Thur 27 Mar

Toxicology Research Laboratory

UIC The University of Illinois at Chicago

Department of Pharmacolcgy (M/C 868)
1940 W. Taylor St.
Chicago. Illinois 60612-7353

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-21
UIC/TRL Study No.: 200

Title Page

Draft Report (Volume 1 of 2)

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

Sponsor: U.S. Army Medical Materiel Development Activity

Test Article: WR238605 Succinate

Contract No.: DAMD17-92-C-2001

Study Director

Debra L. Kirchner, Ph.D., D.A.B.T.

In-Life Phase Completed On

September 18, 1996

Performing Laboratory

TOXICOLOGY RESEARCH LABORATORY (TRL)
University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY Unclassified	3. DISTRIBUTION/AVAILABILITY OF REPORT Unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) UIC/TRL Study No. 200 (UIC-21)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION Toxicology Research Laboratory University of Illinois at Chicago 6b. OFFICE SYMBOL (*If applicable*)	7a. NAME OF MONITORING ORGANIZATION U.S. Army Medical Materiel Development Activity
6c. ADDRESS (*City, State, and ZIP Code*) Department of Pharmacology (M/C 868) 1940 W. Taylor Street Chicago, IL 60612-7353	7b. ADDRESS (*City, State, and ZIP Code*) ATTN: MCMR-RMA-RD Fort Detrick Frederick, MD 21702-5014
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Materiel Development Activity 8b. OFFICE SYMBOL (*If applicable*) MCMR-UMP	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-92-C-2001
8c. ADDRESS (*City, State, and ZIP Code*) Fort Detrick Frederick, MD 21702-5009	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 63807A; PROJECT NO. 30463807; TASK NO. QC; WORK UNIT ACCESSION NO. 073

11. TITLE (*Include Security Classification*)

Oral Prenatal and Postnatal Development Study of WR238605 Succinate in Rats

12. PERSONAL AUTHOR(S)

Levine, Barry S., and Kirchner, Debra L.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (*Year, Month, Day*)	15. PAGE COUNT
Study	FROM 11/15/95 TO _____		

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (*Continue on reverse if necessary and identify by block number*)
FIELD	GROUP	SUB-GROUP	
			WR238605 Pregnancy Lactation Delivery Development of Offspring

19. ABSTRACT (*Continue on reverse if necessary and identify by block number*)

This study evaluated the toxic potential of WR238605 Succinate on the pregnant/lactating female CD® rat (F_0 generation) and the survival and development of their offspring (F_1 generation) consequent to exposure from implantation through weaning. Doses were 2, 6, and 18 mg base/kg/day based on a developmental toxicity study in female CD® rats (UIC/TRL Study No. 154) in which decreased body weight gains and food consumption occurred throughout the study at 30 mg base/kg/day while marginal reductions in body weight and food consumption were noted during the dosing period at 10 mg base/kg/day. In the present study, doses of 2, 6, and 18 mg base/kg/day were administered by daily gavage to female CD® rats (the F_0 generation) for at least 36 days: from gestation day (GD) 0 through postnatal day (PND) 20. The results are summarized in Table 1. There were no mortalities or treatment-related clinical signs or necropsy observations noted in the F_0 generation maternal animals at any dose level. At 18 mg base/kg/day, maternal toxicity was observed as significantly reduced body weights, noted essentially throughout the dosing period (i.e., GD9 - PND21), and significantly reduced food consumption, noted over the gestation period (i.e., GD6 - 20). Significantly reduced food consumption occurred at 6 mg base/kg/day following the initiation of dosing over GD6 - 9; however, body weights were unaffected. Administration of WR238605 Succinate did not affect food consumption or body weights at the low dose. Gestation duration, parturition, and litter size were unaffected by treatment at any dose level. Thus, administration of WR238605 Succinate did not adversely affect the dams' ability to deliver and rear her offspring. Offspring at 18 mg base/kg/day had evidence of growth retardation and slight developmental and functional delays. Adverse findings included significantly reduced body weights in both sexes throughout the pre- and postweaning periods; slight, significantly delayed attainment of eye opening in both sexes; and slight, but significantly decreased rearing activity in females. All other developmental parameters and neuromotor assessments, survival, and attainment of sexual maturity were unaffected at the high dose. No treatment-related effects occurred in any parameter in the F_1 generation at 2 or 6 mg base/kg/day. In conclusion, the no-observable-effect level (NOEL) of WR238605 Succinate on pregnancy, parturition, and lactation in the F_0 generation dams was 18 mg base/kg/day in spite of toxicity observed at this dose level. Based on alterations in body weights, and slight developmental and functional delays at the high dose, the NOEL for the development of the F_1 generation was 6 mg base/kg/day.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS	Unclassified
22a. NAME OF RESPONSIBLE INDIVIDUAL Barry S. Levine	22b. TELEPHONE (*Include Area Code*) (312) 996-5543 22c. OFFICE SYMBOL N/A

STATEMENT OF COMPLIANCE

Study No. 200 entitled "Oral Prenatal and Postnatal Development Study of WR238605 Succinate in Rats" was conducted in compliance with the Good Laboratory Practices regulations as published in 21 CFR 58, 40 CFR 160 and 40 CFR 792 in all material aspects.

The protocol for this study was approved by the UIC Animal Care Committee.

Signature

Study Director

Debra L. Kirchner, Ph.D., D.A.B.T. Date

DRAFT

QUALITY ASSURANCE STATEMENT

STUDY TITLE: ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

STUDY NUMBER: 200

STUDY DIRECTOR: DEBRA L. KIRCHNER

INITIATION DATE: 11/15/95

This study has been divided into a series of phases. Using a random sampling approach, Quality Assurance personnel monitors each of these phases over a series of studies. Procedures, equipment, documentation, etc., are examined in order to assure that the study is performed in accordance with the Good Laboratory Practice regulations of the Food and Drug Administration and the Environmental Protection Agency to assure that the study is conducted according to the protocol.

The following are the inspection dates, phases inspected, and report dates of QA inspections of the study.

INSPECT ON 11/15/95, TO STUDY DIR 11/15/95, TO MGMT 11/15/95
PHASES: PROTOCOL REVIEW

INSPECT ON 4/29/96/96, TO STUDY DIR 4/30/96, TO MGMT 5/1/96
PHASES: ROOM ENVIRONMENT, MORTALITY/MORIBUNDITY, FOOD CONSUMPTION, BODY WEIGHT AND DOSING

INSPECT ON 4/30/96, TO STUDY DIR 4/30/96, TO MGMT 5/1/96
PHASES: CLINICAL SIGNS

INSPECT ON 10/4-7/96, TO STUDY DIR 10/7/96, TO MGMT 10/7/96
PHASES: RAW DATA AND DRAFT REPORT FROM THE ANALYTICAL LAB

INSPECT ON 1/17-27/97, TO STUDY DIR 1/27/97, TO MGMT 1/31/97
PHASES: RAW DATA

INSPECT ON 2/4-7/97, TO STUDY DIR 2/7/97, TO MGMT 2/13/97
PHASES: DRAFT REPORT

Ronald Schoenbeck 2/13/97

QUALITY ASSURANCE **DATE**

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-21
UIC/TRL Study No.: 200

DRAFT

Signature Page

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Sponsor: U.S. Army Medical Materiel
Development Activity
Fort Detrick
Frederick, MD 21702-5009

Test Article: WR238605 Succinate

Sponsor
Representative: George J. Schieferstein, Ph.D.

Testing Facility: Toxicology Research Laboratory (TRL)
University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, Illinois 60612-7353

_____ _____
Debra L. Kirchner, Ph.D., D.A.B.T. Date
Study Director

_____ _____
Barry S. Levine, D.Sc.,Ph.D., D.A.B.T. Date
Principal Investigator

Study Initiation: November 15, 1995

In-Life Inititation: April 23, 1996

Dosing Initiation: April 29, 1996

In-Life Completion: September 18, 1996

DRAFT

TABLE OF CONTENTS

VOLUME 1 OF 2

TABLE OF CONTENTS (Continued)

TABLES

APPENDICES

VOLUME 2 OF 2

DRAFT

1. SUMMARY

This study evaluated the toxic potential of WR238605 Succinate on the pregnant/lactating female CD® rat (F_0 generation) and the survival and development of their offspring (F_1 generation) consequent to exposure from implantation through weaning. Doses were 2, 6, and 18 mg base/kg/day based on a developmental toxicity study in female CD® rats (UIC/TRL Study No. 154) in which decreased body weight gains and food consumption occurred throughout the study at 30 mg base/kg/day while marginal reductions in body weight and food consumption were noted during the dosing period at 10 mg base/kg/day.

In the present study, doses of 2, 6, and 18 mg base/kg/day were administered by daily gavage to female CD® rats (the F_0 generation) for at least 36 days: from gestation day (GD) 0 through postnatal day (PND) 20. The results are summarized in Table 1. There were no mortalities or treatment-related clinical signs or necropsy observations noted in the F_0 generation maternal animals at any dose level. At 18 mg base/kg/day, maternal toxicity was observed as significantly reduced body weights, noted essentially throughout the dosing period (i.e., GD9 - PND21), and significantly reduced food consumption, noted over the gestation period (i.e., GD6 - 20). Significantly reduced food consumption occurred at 6 mg base/kg/day following the initiation of dosing over GD6 - 9; however, body weights were unaffected. Administration of WR238605 Succinate did not affect food consumption or body weights at the low dose. Gestation duration, parturition, and litter size were unaffected by treatment at any dose level. Thus, administration of WR238605 Succinate did not adversely affect the dams' ability to deliver and rear her offspring.

Offspring at 18 mg base/kg/day had evidence of growth retardation and slight developmental and functional delays. Adverse findings included significantly reduced body weights in both sexes throughout the pre- and postweaning periods; slight, significantly delayed attainment of eye opening in both sexes; and slight, but significantly decreased rearing activity in females. All other developmental parameters and neuromotor assessments, survival, and attainment of sexual maturity were unaffected at the high dose. No treatment-related effects occurred in any parameter in the F_1 generation at 2 or 6 mg base/kg/day. In conclusion, the no-observable-effect level (NOEL) of WR238605 Succinate on pregnancy, parturition, and lactation in the F_0 generation dams was 18 mg base/kg/day in spite of toxicity observed at this dose level. Based on alterations in body weights, and slight developmental and functional delays at the high dose, the NOEL for the development of the F_1 generation was 6 mg base/kg/day.

2. INTRODUCTION

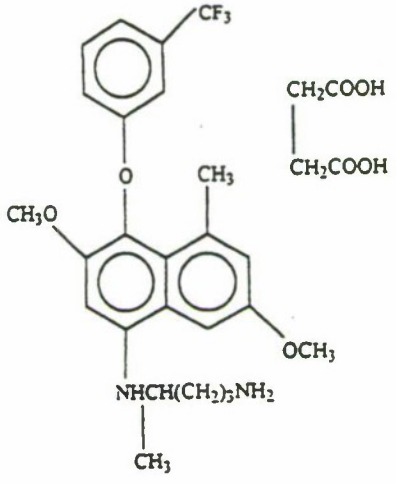
This study was conducted to evaluate the toxic potential of the test article on the pregnant/lactating female rat (F_0 generation) and the survival and development of their offspring (F_1 generation) consequent to exposure from implantation through weaning. WR238605 Succinate is being developed at an antimalarial agent. The test article was administered by daily gavage to female CD® rats (the F_0 generation) for at least 36 days, i.e., from GD6 through PND20. All methods and procedures were conducted in accordance with the Toxicology Research Laboratory Quality Assurance Programs designed to conform with FDA Good Laboratory Practices Regulations. No unforeseen circumstances affected the integrity of the study. This study was initiated on November 15, 1995; dosing began on April 14 and 15, 1996 (first shipment) and May 13 and 14, 1996 (second shipment). The in-life portion was terminated on September 18, 1996 (last F_1 generation necropsy).

DRAFT

3. MATERIALS AND METHODS

3.1 Test Article

WR238605 Succinate (Bottle No. BM12562) a yellow powder, was provided by the Sponsor and was received November 9, 1995 from Herner and Co., Rockville, MD. The test article was previously assigned an in-house chemical number (0720614). The chemical name of the test article is 8-[(4-Amino-1-methylbutyl)amino]-2,6-dimethoxy-4 methyl-5-(3-trifluoromethyl phenoxy)quinoline succinate, and the mole fraction of the base is 0.8. It was stored at 0 to 4° C at ambient relative humidity in an amber bottle. The chemical structure follows.



The Analytical Chemistry Report is contained in Appendix 1. The test article was initially identified by GS-MS and the purity, as determined by HPLC, was 99.98 ± 0.00%. The terminal purity was 99.81 ± 0.03%. Thus, the test article was stable under storage conditions.

3.2 Animals

One-hundred and twenty eight time-mated nulliparous female CD® Virus Antibody Free rats (GD0 = day of vaginal plug detection) were obtained from Charles River Breeding Laboratories (Portage, MI) in two shipments (April 26, 1996 and on May 10, 1996) with two successive GD0 dates per shipment (i.e., a total of four GD0 subsets). The animals were approximately 10 weeks old (dates of birth February 16, 1996 and March 1, 1996, respectively) upon arrival at the UIC AAALAC-accredited animal facility. Each F_0 generation female was given a facility-unique animal number by the supplier (ear tag) and a separate study-unique number as a subcutaneously implanted microchip upon arrival at UIC. This latter number appeared on a cage card visible on the front of each cage. The cage card additionally contained the study number, test article identification, treatment group number, sex, and dose level. Cage cards were color-coded as a function of treatment group. Animals from the first shipment were maintained in one room at the UIC AAALAC-accredited animal facility, while animals from the second shipment

(received two weeks later) were housed in a separate, adjacent room. All rats were singly housed (except during portions of the postnatal period when dams and their litters were cohoused) in polycarbonate cages with Anderson bed-o-cob® bedding (Heinold, Kankakee, IL) in a temperature (65 - 78°F) and humidity (30 - 70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm^2 area and 20 cm height, was adequate to house rats at the upper weight range as described in the *Guide for the Care and Use of Laboratory Animals*, DHHS (NIH) No. 86.23. All animals were routinely transferred to clean cages with fresh bedding weekly.

Certified Rodent Chow No. 5002 (PMI Feeds Inc., St. Louis, MO) was provided *ad libitum* as a powder from arrival to parturition in order to measure F_0 generation food consumption. The pelleted form of the chow was provided *ad libitum* from parturtion to termination. Tap water from an automatic watering system in which the room distribution lines were flushed daily was provided *ad libitum* from arrival until termination. The water was not treated with additional chlorine or HCl. There were no known contaminants in the feed or water which were expected to influence the study. A copy of the feed certification was kept with the study records. The results of the most current chemical analyses of Chicago water conducted by the City of Chicago are documented in files maintained by Quality Assurance.

3.3 Experimental Design

F_0 GENERATION

The F_0 generation animals were quarantined for at least 3 days, from receipt until dosing was initiated on GD6. During the quarantine period, the animals were observed daily for signs of illness, and all unusual observations were documented and reported to the Study Director or Clinical Veterinarian. Animals were examined during quarantine and were approved for use by the Clinical Veterinarian prior to being placed on test. All animals were released from quarantine for use on the study. Prior to the initiation of dosing, animals from each of the four GD0 subsets were separately randomized using a computer-generated randomization program, stratified on the basis of body weight, to result in a total of 6 or 7 animals/group/day for a total of 25 animals/group. The thirty eight animals not assigned to the study were euthanized via CO_2 asphyxiation and discarded.

Group	No. of F_0 Females	Treatment	Dose Level (mg base/kg/day)	Dose Conc. (mg base/ml)	Dose Volume (ml/kg/day)
1	25	Vehicle	0	0	5
2	25	WR238605	2	0.4	5
3	25	WR238605	6	1.2	5
4	25	WR238605	18	3.6	5

Dose levels were selected on the basis of a developmental toxicity study in female rats (UIC/TRL Study No. 154). The number of F_0 animals, 25/sex/dose level, was necessary

to result in 16 - 20 litters/group for rodents as recommended in the *ICH Harmonized Tripartite Guidelines* (1993).

The gavage procedure was accomplished by the use of a rigid oral feeding needle. The test article dosing suspensions were administered daily to the F_0 generation females from GD6 through PND20 for a total of at least 36 days.

Test article dosing suspensions were prepared weekly by adding the appropriate amount of WR238605 Succinate (adjusted for the mole fraction and for purity) with the required volume of control article (1.0% Methylcellulose/0.2% Tween 80) in a precalibrated beaker. The contents were mixed with an Omni-Mixer homogenizer for at least 5 minutes. The control suspensions were also prepared weekly. Both the test article and the control suspensions were administered to the animals at a dosing volume of 5 ml/kg/day. The dosing suspensions (including controls) were stored at 2 - 8° C. All suspensions were allowed to warm to room temperature and stirred continuously before and during gavage administration. Samples of all dosing suspensions were analyzed prior to use and only suspensions within 10% of their target concentration were used. Samples of test article and control suspensions were also analyzed weekly after use. Stability data obtained from previous study (UIC/TRL Study No. 047) indicated that the formulations of WR238605 Succinate were stable for 28 days. The test article suspensions were considered to be homogeneous based on homogeneity data also obtained from UIC/TRL Study No. 047.

Body weights were recorded for all animals on GD0 (by the supplier) and on GD5 (randomization), GD6, 9, 12, 15, 18 and 20; and on PND0, 4, 7, 10, 14, 17 and 21. Food consumption was measured for all study animals during the intervals for GD6 - 9, 9 - 12, 12 - 15, 15 - 18, and 18 - 20. Animals were observed daily for signs of clinical toxicity approximately 1 -2 hours after dosing. Animals were also observed twice daily (at least six hours apart) for moribundity/mortality.

Beginning on GD18, the F_0 dams were observed at least twice daily for signs of parturition. The day of parturition was designated PND0. The lactation period was from PND0 to 21 during which time the dam and litter remained housed together. One female (Dam No. 159 at 6 mg base/kg/day) failed to deliver and was euthanized by CO_2 asphyxiation and grossly examined externally and internally on presumed GD25.

At the end of the postnatal period (i.e., on PND21), the dams were euthanized by CO_2 asphyxiation and grossly examined externally and internally. The thoracic, abdominal, and pelvic cavities were opened, and the viscera examined. Organs/tissues with gross lesions were preserved in 10% neutral buffered formalin for possible histopathologic examination. Corresponding organs/tissues from two control animals were also retained for comparison. Upon issuance of the final report, the Sponsor will provide written directions regarding the disposition of tissues not examined histopathologically.

F_1 GENERATION

On PND0 (PND1 for pups from litter No. 138) each pup in the litter was identified using toe clipping. On PND4, litters were culled in order to equalize the burden on the dam

for milk production and to diminish confounding effects on pup growth and development. When possible, the litters were culled via a computer randomization procedure using random numbers to yield a maximum of 4 pups/sex/litter (i.e., a maximum of 8 pups/litter). All other pups were euthanized via an intraperitoneal (IP) injection of 40% sodium pentobarbital (≈ 0.04 ml/fetus), examined externally, and discarded.

The pups were sexed on PND0, 4, 7, 14 and 21. The numbers of stillborn (PND0 only), dead, or cannibalized pups were recorded. Stillborn pups were not sexed. If a pup was not found on PND4, 7, 14, or 21, it was recorded as missing. Missing pups were presumed to have been completely cannibalized by the dam. Clinical signs were recorded as observed PND0, 4, 7, 14, and 21 and weekly thereafter. The pups were observed twice daily for mortality from PND0 until termination.

Individual body weights were recorded on PND0, 4 (precull), 7, 14, and 21 during the preweaning period. During the postweaning period, body weights were recorded weekly from PND28 until study termination. Because of the stagger-start design of the study, the F_1 generation animals were delivered, evaluated, and sacrificed in two subsets resulting in a staggered study termination. Body weights were recorded from PND70 - 91 for all of the F_1 generation animals selected for the postweaning fertility phase. Subsequently, these animals were necropsied between PND91 and 119. Thus, PND91 was considered to be the termination body weight day.

F_1 generation preweaning developmental parameters were observed daily in all pups until present (i.e., attained) in accordance with the following schedule.

Parameter	Observation Began on Postnatal Day:
Surface Righting Reflex	1
Incisor Appearance	7
Eyes Open	10
Cliff Avoidance	15

F_1 pups were weaned on PND21 (i.e, the F_0 females were removed from the cage, euthanized and necropsied), and a maximum of two animals/sex/litter, when possible, were selected to remain on study. These two animals/sex were, when possible, the same first two pups/sex that were randomly retained on PND4. All F_1 animals retained during the postweaning period were assessed in a functional observational battery (FOB) for weanling rats and were evaluated for the attainment of postweaning developmental parameters and for motor activity in an open-field. One animal/sex/litter was randomly selected for assessment of learning and memory via a passive avoidance method, and the other animal/sex/litter was used to assess fertility indices. There was only one female in litter No. 109 (0 mg base/kg/day). This female was assigned to all postweaning evaluations. Animals not selected for postweaning assessments were euthanized via CO_2 asphyxiation, examined externally, and discarded. After the start of the F_1 fertility phase, all F_1 animals not selected for fertility assessment were similarly euthanized, examined, and discarded.

The F_1 animals retained at the time of weaning were individually housed and given a study-unique number as a subcutaneously implanted microchip. A record was maintained correlating the toe-mark ID with the study-unique ID for each animal. The study-unique number also appeared on a cage card visible on the front of each cage. The cage card additionally contained the study number, test article identification, treatment group number, sex, and dose level. Cage cards were color-coded as a function of treatment group.

An FOB for weanling rats was conducted in the morning (before 1300) on postnatal days 28 ± 2. The FOB consisted of a series of observations of the animals in their homecage, when handled, and in an open field and an evaluation of selected reflexes and physical measures. These data were used to provide an assessment of the overall development, behavior, and general functional integrity of the animals' central and autonomic nervous systems (Moser, *et al.*, 1988; Weisenburger, 1995).

Postweaning developmental parameters were observed until present (i.e., attained) in accordance with the following schedule:

Parameter:	Observation Began on Postnatal Day:
Vaginal Opening (females)	28
Preputial Separation (males)	35

General locomotor activity and patterns of exploratory behavior were evaluated in selected F_1 animals (Walsh and Cummins, 1976; Fitzgerald, *et al.*, 1988; Weisenburger, 1995). The animals were assessed one at a time on postnatal days 42 ± 2 using the Flex-Field Activity System® (San Diego Instruments, San Diego, CA). The selected animals were placed in a clear acrylic 16" x 16" enclosure for 20 minutes. Photobeam disruptions were used to quantitate (i.e., score) central and peripheral horizontal activity and rearing (i.e., vertical) activity within the enclosure. These data were then organized to allow analyses of the animals' active time in the horizontal plane, total time spent in the center of the enclosure, and total time spent in the rearing position.

Acquisition of a behavior (i.e., learning) and retention of the new behavior (i.e., memory) were evaluated in selected F_1 animals (Riekkinen, *et al.*, 1990; Weisenburger, *et al.*, 1995). The animals were placed one at time in the Gemini Avoidance System® (San Diego Instruments, San Diego, CA) selected for the passive avoidance/trials to criterion test. This test assessed the animal's ability to avoid the preferred darkened chamber using negative reinforcement and was conducted in two phases:

Phase:	Postnatal Day:
Acquisition (learning)	56 ± 2
Retention (memory)	63 ± 2

For each phase, the animals were assessed one at a time in an enclosure with two chambers, one illuminated and one dark, separated by a metal wall with a sliding door. During the acquisition phase of the test, the animal was allowed to cross from the illuminated chamber (Trial 1). The door would automatically close, and a pulse of

negative reinforcement was delivered to the floor grid. The animal was returned to the illuminated side and allowed to choose to remain there or "cross over" into the dark chamber (Trial 2) If the animal crossed over, a negative reinforcement was again delivered to the floor grid. The number of seconds that the animals remained in the illuminated chamber before crossing over to the darkened chamber, termed "latency", was recorded. If the latency was less than 180 seconds, the animal was retested. Acquisition was achieved when the animal remained in the illuminated chamber for 180 seconds. The number of trials to acquisition was also recorded. The retention phase, conducted one week later, consisted of one trial without negative reinforcement. Again, the latency times (i.e., the number of seconds the animal remained in the illuminated chamber) were recorded.

The rats selected for the assessment of fertility were sexually mature (i.e., at least 10 weeks of age) at the initiation of mating. During the 14 day cohabitation period, females were paired with males from the same treatment group. Sibling pairings were avoided. Vaginal washings were performed each morning during the cohabitation period in order to determine if mating had occurred. When a vaginal plug or the presence of sperm in the vaginal washing was observed (defined as GD0), the mating pair was separated by returning the female to her individual cage. Females that did not show evidence of mating at the end of the cohabitation period were separated from their mate and returned to their cage.

Each female was observed at least twice daily for signs of parturition beginning on gestation day 18, and the day of parturition was recorded. On the day parturition was observed, the numbers of viable and stillborn F_2 pups were recorded. Observations of external abnormalities were recorded. Viable F_2 pups were euthanized via an intraperitoneal injection of 40% sodium pentobarbital ($\approx$ 0.04 ml/fetus) and discarded. Stillborn F_2 pups were also discarded. Females that did not display evidence of mating were euthanized and necropsied 25 days after the last day of cohabitation. Uteri with no macroscopic implantation were opened and placed for approximately 10 minutes in aqueous ammonium sulfide solution (10%). Any resorptions noted were graded (early or late), counted, and recorded.

Following a review by the Study Director and Sponsor's Representative, the F_1 animals used during the fertility phase were euthanized via CO_2 asphyxiation, examined externally, and discarded. These animals were grossly examined externally at the time of sacrifice, and any abnormalities were recorded. Skin tissues from two males at 2 mg base/kg/day (Animal Nos. 1267 and 1493) and the eye from one female at 18 mg base/kg/day (Animal No. 18911) were preserved in 10% neutral buffered formalin for possible histopathologic examination. Skin tissue from a male control (Animal No. 10103) was also retained for comparison. Upon issuance of the final report, the Sponsor will provide written directions regarding the disposition of tissues not examined histopathologically.

3.4 Statistical Analyses

One-way analyses of variance (ANOVA) was used to analyze F_0 and F_1 generation body weights, body weight gains, and gestation duration; F_0 generation food consumption; F_1 generation motor activity; and the number of viable pups in the F_1 and F_2 generations.

If a significant F ratio was obtained ($p \leq 0.05$), Dunnett's test was used for pair-wise comparisons to the control group. The Kruskal-Wallis test was used to analyze F_1 generation attainment of developmental parameters, passive avoidance retention, and the number stillborn pups in the F_1 and F_2 generations. If a significant F ratio was obtained ($p \leq 0.05$). the Mann/Whitney U test was used for pair-wise comparisons to the control group. Parameters recorded during conduct of the F_1 generation FOB were analyzed by one-way ANOVA (count and interval data and air righting reflex), the Kruskal-Wallis test (rank data), or the Chi-Square test (quantal and descriptive data and palpebral closure). Pair-wise comparisons to the control group were not conducted since there were no significant F ratios ($p \leq 0.05$). F_1 generation sex ratios (PND0) and mating* and fertility** indices were analyzed by the Chi-Square test. Pair-wise comparisons to the control group were not conducted since there were no significant F ratios ($p \leq 0.05$).

*Mating Index = (No. with evidence of mating/No. cohoused) X 100
**Fertility Index = (No. pregnant/No. with evidence of mating) X 100

The litter was the experimental unit for the statistical analysis of F_1 generation preweaning parameters for body weight, body weight gains, attainment of developmental landmarks, and number of viable and stillborn pups (Haseman and Hogan, 1975; Nishimura and Kast, 1989). Thus, the group means were derived in two steps. First, the data for the individual pup was used to determine the mean for each litter. Second, the litter means were used to determine the mean for each group. For all other analyses of F_0 and F_1 generation data, the individual animal was the experimental unit.

4. RESULTS

4.1 Dosage Formulation Analyses

The results of the dosage formulations analyses are shown in Table 2. The Analytical Chemistry Report is in Appendix A.

All analyzed dosing solutions which were used were within 10% of their target concentration.

4.2 F_0 Generation

4.2.1 Mortality/Clinical Signs

The summary of the F_0 generation clinical signs are presented in Table 3. Individual clinical signs are in Appendix B.

There were no mortalities and no clinical signs noted at any dose level following oral administration of WR238605 Succinate during gestation or lactation. During the postnatal period, no unusual nursing or nesting behaviors were observed indicating that the dams in all WR238605 Succinate-treated groups were fully able to rear their offspring until weaning.

4.2.2 Body Weights

The summaries of the F_0 generation body weights and weight gains are in Tables 4 and 5, respectively. Individual body weight data are included in Appendix C.

At 18 mg base/kg/day, body weights were significantly reduced following initiation of treatment through the end of the dosing period (i.e., GD9 - PND21). These alterations were attributed to an initial, significant reduction in body weight gains noted during GD6 - 15. Although high dose animals gained weight at the same rate as the control animals for the rest of the dosing period (i.e., GD15 - PND21), body weights remained significantly reduced. At the end of the preweaning period during PND17 - 21, body weight gain was significantly increased in high dose females compared to weight loss noted in females in the 0, 2, and 6 mg base/kg/day groups. Total body weight gain for the gestation and postnatal period was significantly decreased at 18 mg base/kg/day compared to the controls. There were no effects of treatment on body weights at 2 or 6 mg base/kg/day. Slight but significant body weight reductions at 6 mg base/kg/day on PND4 and 10 and at 2 mg base/kg/day on PND17 observed in the absence of any other alterations were considered not biologically meaningful.

4.2.3 Food Consumption

The summary of the F_0 generation food consumption is presented in Table 6. Individual food consumption data are shown in Appendix D.

At 18 mg base/kg/day, food consumption was significantly reduced over all intervals during the gestation period. At 6 mg base/kg/day, a significant reduction in food consumption occurred over GD6 - 9; food consumption for the remainder of the gestation period was comparable to the controls. There were no effects of treatment on food consumption at 2 mg base/kg/day.

4.2.4 Reproductive Parameters

The summary of the F_0 generation reproductive parameters are presented in Table 7. Individual data are included in Appendices E and I.

Administration of WR238605 Succinate had no affects on gestation duration or parturition. The number of viable litters and the number of males and females per litter on PND0 were also comparable among the groups.

4.2.5 Gross Necropsy Observations

The summary of the F_0 generation gross necropsy observations are presented in Appendix F.

One dam (No. 159) at 6 mg base/kg/day was palpated not pregnant and sacrificed on her GD25. No gross necropsy observations were recorded for this animal. All of the other dams survived until scheduled necropsy on PND21. There were no treatment-related gross necropsy observations at any dose level.

4.3 F_1 Generation

4.3.1 Mortality/Clinical Observations

The summary of the F_1 generation postweaning clinical signs for males and females are presented in Tables 8.1 and 8.2, respectively. Individual clinical signs for the litters evaluated during the preweaning period and the animals evaluated during the postweaning period are in Appendix G.

There were no treatment-related mortalities or clinical signs observed in the F_1 generation during the postnatal period. During the preweaning period on PND 7, 14, or 21, a few pups in all groups including the controls were missing (i.e., not found in the cage). These pups were considered to have died and been cannibalized, a typical occurrence in rodent litters. During the postweaning period, observations of dehydration or dark material around the eyes noted in 1 or 2 animals in all groups including the controls were considered sporadic and unrelated to treatment.

4.3.2 Body Weights

The summaries of the F_1 generation body weights and weight gains for the preweaning period are in Tables 9.1 and 10.1, respectively, for males and Tables 9.2 and 10.2, respectively for females. The summaries of the F_1 generation body weights and weight gains for the postweaning period are in Tables 11.1 and 12.1, respectively, for males and Tables 11.2 and 12.2, respectively for females. Individual body weight data for the preweaning and postweaning periods are included in Appendix H.

At 18 mg base/kg/day, body weights on PND0 (i.e, birth weights) were significantly reduced in both sexes. During the preweaning period, the rate of body weight gain was also reduced in both sexes at the high dose resulting in significantly reduced body weights on all evaluated days. Although statistically insignificant, total body weight gain for the preweaning period was reduced in both sexes. There were no adverse effects on body weight gains at 2 and 6 mg base/kg/day during the preweaning period.

During the postweaning period, body weight gains were comparable among all groups. However, the body weights were significantly decreased in high dose males from PND 28 - 70 and in high dose females from PND 28 - 56. Body weights after these timepoints to the end of the study were slightly but

insignificantly reduced compared to the controls. There were no treatment-related effects on body weights at 2 or 6 mg base/kg/day. Isolated but significantly increased body weights observed on one occasion in males and in females at 2 mg base/kg/day were not considered biologically relevant.

4.3.3 Preweaning Survival

The summary of the F_1 generation preweaning survival is presented in Table 13. Individual survival data for the F_1 pups are in Appendix I.

Preweaning survival was not affected in any WR238605 Succinate group. There were no group differences in the number of litters and number of viable pups of both sexes per litter pre- or post cull.

4.3.4 Developmental Parameters

The summary of the F_1 generation developmental parameters is presented in Table 14. Individual data are in Appendix J.

All evaluated F_1 generation offspring attained all of the developmental parameters. However, the mean day of appearance for "eyes open" was significantly delayed in both sexes at 18 mg base/kg/day. Generally, eyes were opened by PND14; however, this parameter was attained on PND15 for many pups at the high dose. There were no affects on the mean day of appearance of any other developmental parameter.

4.3.5 Functional Observation Battery (FOB)

The summary of the F_1 generation FOB is presented in Table 15. Individual animal data are presented in Appendix K.

Significantly reduced body weights were noted in both sexes at 18 mg base/kg/day. All other parameters were comparable among groups indicating the general development, behavior, and functional integrity of the F_1 animals' nervous systems were not affected by treatment.

4.3.6 Motor Activity

The summary of the F_1 generation motor activity assessment is presented in Table 16. Individual animal data are in Appendix L.

Females at 18 mg base/kg/day spent significantly less time rearing (i.e., both front paws off the floor of the enclosure) during the twenty minutes spent in the enclosure. There were no differences in the amount time spent in the horizontal plane or in the center of the enclosure in any treated groups.

4.3.7 Learning and Memory

The summary of the F_1 generation passive avoidance learning (i.e., acquisition) and memory (i.e., retention) are presented in Table 17. Individual animal data are presented in Appendix M.

Essentially all animals completed the acquisition phase of the passive avoidance test within two or three trials. The first trial was not completed by one male each at 2 and 6 mg base/kg/day. Since these two animals never crossed from the illuminated to the dark chamber of enclosure, they were not considered to have had an opportunity to "learn". During the retention phase, the latency times (i.e., the average time the animals remained in the darkened chamber) were not significantly different between the groups.

4.3.8 Reproductive Parameters and Gross Necropsy Observations

The summary of the F_1 generation reproductive parameters is presented in Table 18. Individual data are in Appendix N.

There were no adverse effects at any dose level on gestation duration, mating and fertility indices, or the number of viable or stillborn F_2 generation pups.

5. DISCUSSION

The present study evaluated the toxic potential of WR238605 Succinate on the pregnant/lactating female (F_0 generation) and the survival and development of their offspring (F_1 generation) consequent to exposure from implantation through weaning. Doses of 2, 6, and 18 mg base/kg/day were administered by daily gavage to female CD® rats (the F_0 generation) for at least 36 days: from GD6 through PND20. The results are summarized in Table 1.

There were no mortalities or treatment-related clinical signs or necropsy observations noted in the F_0 generation maternal animals at any dose level. At 18 mg base/kg/day, maternal toxicity was observed as significantly reduced body weights, noted essentially throughout the dosing period (i.e., GD9 - PND21), and significantly reduced food consumption, noted over the gestation period (i.e., GD6 - 20). Significantly reduced food consumption occurred at 6 mg base/kg/day following the initiation of dosing over GD6 - 9; however, body weights were unaffected. Administration of WR238605 Succinate did not affect body weights or food consumption at the low dose.

In the present study, the dams were allowed to deliver and rear their offspring. Treatment with WR238605 Succinate did not affect reproductive functions at any dose level. Gestation duration, parturition, and nesting behaviors were similar among all groups. At the end of the preweaning period, weight gain was significantly increased in high dose females compared to weight loss

noted in females in the control, low, and mid dose. The biological relevance of this alteration is unclear. It is possible that the high dose dams were still producing milk or perhaps the pups had not depleted the milk reserves. Milk production or specific maternal-litter interactions were not evaluated in this study.

There was no effect of treatment on viability at birth or survival during the preweaning period indicating that adaptation to extrauterine life was not compromised at any dose level. Pups of both sexes at 18 mg base/kg/day were born with significantly reduced weights compared to controls. Additionally, the rate of growth was significantly reduced throughout the preweaning period in high dose male and female pups. A significant delay in attainment of eye opening was also noted during preweaning in both sexes at 18 mg base/kg/day. F_1 generation body weights at 18 mg base/kg/day remained significantly reduced (until PND70 in males and PND49 in females) even though their rate of growth was comparable to the controls. Based on the findings from the FOB, there were no effects of treatment on general patterns of gait and overall reactivity or excitability. However, during assessment of motor activity, high dose females spent significantly less time in a rearing posture. These animals did not display gait anomalies or problems with coordination and balance during conduct of the FOB or at any other time during the study. It is possible that muscle strength was diminished in high dose females. Rearing is also considered by some investigators as a nonspecific indicator excitability or curiosity related to hippocampal brain wave activity (Walsh and Cummins, 1976). However, there were no other behavioral alterations, i.e., no indications of stress or fear as assessed in the FOB or other components of the motor activity test. Thus, while the results of the motor activity assessment suggests the presence of a functional deficit, the biological relevance of the finding is unclear. There were no affects on attainment of preputial separation or vaginal opening, hormonally mediated developmental landmarks indicative of sexual maturity, and no adverse findings observed during the F_1 generation fertility assessment. No treatment-related effects occurred in any parameter in the F_1 generation at 2 or 6 mg base/kg/day.

In conclusion, the no-observable-effect level (NOEL) of WR238605 Succinate on pregnancy, parturition, and lactation in the F_0 generation dams was 18 mg base/kg/day in spite of toxicity observed at this dose level. Based on alterations in body weights, and slight developmental and functional delays at the high dose, the NOEL for the development of the F_1 generation was 6 mg base/kg/day.

6. REFERENCES

Fitzgerald, RE, Berres, M and Schaeppi (1988). Validation of a photobeam system for assessment of motor activity in rats. Toxicology 49:433-439.

Haseman, JK and Hogan, MD (1975). Selection of the experimental unit in teratology studies. Teratology 12:165-172.

Moser, VC, McCormick, JP, Creason, JP, and MacPhail, RC (1988). Comparison of chlordimeform and carbaryl using a functional observational battery. Fund. Appl. Tox. 11:189-206.

Nishimura, M and Kast, A (1989). Analysis of historical control litter parameters of reproduction toxicity studies in Sprague-Dawley derived rats. Exp. Anim. 38:127-133.

Riekkinen Jr., P, Sirvio, J. Aaltonen, M, and Riekkinen, P (1990). Effects of concurrent manipulations of nicotinic and muscarinic receptors on spatial and passive avoidance learning. Pharmacol. Biochem. Behav. 37:405-410.

Walsh, RN and Cummins, RA (1976). The open-field test: A critical review. Psychological Bulletin 83: 482-504.

Weisenburger, WP (1995). Neurobehavioral methods in the safety evaluation of drugs and chemicals. Lab Animal 2: 24-31

7. PERSONNEL

Study Director	Debra L. Kirchner, Ph.D., D.A.B.T.
Principal Investigator	Barry S. Levine, D.Sc., D.A.B.T.
Clinical Veterinarian	James Artwohl, D.V.M., M.S., D.A.C.L.A.M.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Nancy Dinger, B.S.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

Report preparation was assisted by Mukesh Pitroda, B.A., Nancy Dinger, B.S., and Lisa Feichter, B.S.

8. ARCHIVES

The raw data, specimens, test article reserves, and final report are archived at the Toxicology Research Laboratory (TRL), University of Illinois at Chicago (UIC), Department of Pharmacology, 1940 W. Taylor St., Chicago, IL 60612-7353.

Table 1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

Summary of Toxic Responses

Dose Level (mg base/kg/day)	0	2	6	18
F_0 Generation:				
No. Pregnant/On Study	25/25	25/25	24/25	25/25
Clinical Signs	-	NE	NE	NE
Body Weight	-	NE	NE	↓
Food Consumption	-	NE	NE	↓
Reproductive Indices	-	NE	NE	NE
F_1 Generation:				
Clinical Signs: Males/Females	-	NE/NE	NE/NE	NE/NE
Preweaning Survival: Males/Females	-	NE/NE	NENE	NE/NE
Body Weight: Males/Females	-	NE/NE	NE/NE	↓/↓
Developmental Landmarks: Males/Females	-	NE/NE	NE/NE	↑ EO/↑ EO
Functional Observational: Battery Males/Females	-	NE/NE	NE/NE	NE/NE
Motor Activity: Males/Females	-	NE/NE	NE/NE	NE/↓ R
Learning/Memory: Males/Females	-	NE/NE	NE/NE	NE/NE
Reproductive Assessment	-	NE	NE	NE

CONCLUSION:
This study evaluated the toxic potential of WR238605 Succinate in the pregnant and lactating CD® female rat (F_0 Generation) and the survival and development of their offspring (F_1 generation) consequent to exposure from implantation through weaning. Doses were 2, 6, and 18 mg base/kg/day administered to the F_0 generation dams from GD6 - PND20 (GD0 = day of vaginal plug). There were no mortalities and no treatment-related clinical signs or gross necropsy observations at any dose level. At 18 mg base/kg/day, maternal toxicity was as significantly reduced body weights for essentially the entire dosing period (i.e., GD9 - PND21) and significantly reduced food consumption noted over the gestation period (i.e., GD6 - 20). Significantly reduced food consumption occurred at 6 mg base/kg/day following the initiation of dosing over GD6 - 9; however, body weights were unaffected. Gestation duration, parturition, and litter size were unaffected by treatment at any dose level. Thus, administration of WR238605 Succinate did not adversely affect the dams' ability to deliver or rear her offspring. The F_1 offspring at 18 mg base/kg/day had evidence of growth retardation and slight developmental and functional delays. Adverse findings included significantly reduced body weights in both sexes throughout the preweaning and postweaning periods; slight, significantly delayed attainment of eye opening in both sexes; and slight, but significantly decreased rearing activity in females. All other developmental parameters and neuromotor assessments, survival, and attainment of sexual maturity were unaffected at the high dose. No treatment-related effects occurred in any parameter in the F_1 generation at 2 or 6 mg base/kg/day. In conclusion, the no-observable-effect level (NOEL) of WR238605 Succinate on pregnancy, parturition, and lactation in the F_0 generation dams was 18 mg base/kg/day in spite of toxicity observed at this dose level. Based on alterations in body weights, and slight developmental and functional delays at the high dose, the NOEL for the development of the F_1 generation was 6 mg base/kg/day.

NE = No Effect EO = Increased attainment of eye opening R = Rearing component

Table 2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Dosage Formulations Analyses

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
1	0.0	04/25/96	0	-	05/02/96	0	-
	0.4		0.398 ± 0.003	99.5		0.402 ± 0.003	101.0
	1.2		1.135 ± 0.048	94.6		1.178 ± 0.004	103.8
	3.6		3.618 ± 0.047	100.5		3.659 ± 0.045	101.1
2	0.0	05/02/96	0	-	05/09/96	0	-
	0.4		0.398 ± 0.002	99.5		0.397 ± 0.002	99.7
	1.2		1.188 ± 0.010	99.0		1.195 ± 0.004	100.6
	3.6		3.703 ± 0.010	102.9		3.730 ± 0.026	100.7
3	0.0	05/09/96	0	-	05/16/96	0	-
	0.4		0.396 ± 0.003	99.0		0.391 ± 0.003	98.7
	1.2		1.213 ± 0.010	101.1		1.186 ± 0.005	97.8
	3.6		3.684 ± 0.047	102.3		3.702 ± 0.020	100.5
4	0.0	05/16/96	0	-	05/23/96	0	-
	0.4		0.403 ± 0.004	100.8		0.425 ± 0.027	105.5
	1.2		1.219 ± 0.010	101.6		1.212 ± 0.006	99.4
	3.6		3.603 ± 0.154	100.1		3.745 ± 0.056	103.9
5	0.0	05/23/96	0	-	05/30/96	0	-
	0.4		0.420 ± 0.021	105.0		0.394 ± 0.004	93.8
	1.2		1.209 ± 0.022	100.8		1.211 ± 0.018	100.2
	3.6		3.662 ± 0.021	101.7		3.621 ± 0.075	98.9
6	0.0	05/30/96	0	-	06/06/96	0	-
	0.4		0.396 ± 0.004	99.0		0.408 ± 0.006	103.0
	1.2		1.223 ± 0.011	101.9		1.190 ± 0.010	97.3
	3.6		3.719 ± 0.041	103.3		3.675 ± 0.055	98.8
7	0.0	06/06/96	0	-	06/13/96	0	-
	0.4		0.400 ± 0.003	100.0		0.401 ± 0.002	100.3
	1.2		1.200 ± 0.030	100.0		1.210 ± 0.017	100.8
	3.6		3.629 ± 0.188	100.8		3.634 ± 0.188	100.1
8	0.0	06/13/96	0	-	06/20/96	0	-
	0.4		0.407 ± 0.003	101.8		0.394 ± 0.005	96.8
	1.2		1.149 ± 0.039	95.8		1.144 ± 0.029	99.6
	3.6		3.646 ± 0.131	101.3		3.714 ± 0.031	101.9

Table 3

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 200 (F_0 Generation) SEX: FEMALE

DOSE:	0	2	6	18 (mg base/kg/day)
GROUP:	1-F	2-F	3-F	4-F
Scheduled Sacrifice	25	25	24	25
Normal	25	25	25	25
Sacrificed [a]	0	0	1	0
Total Number of Animals	25	25	25	25

[a]Dam No. 159 at 6 mg base/kg/day was not pregnant and was sacrificed on GD25.

Table 4

DRAFT

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 200 (F_0 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 4-F	(mg base/kg/day)
GD 0	MEAN	201	201	203	202	
	S.D.	5.0	4.7	4.7	5.1	
	N[a]	25	25	24	25	
GD 5	MEAN	233	233	234	234	
	S.D.	7.6	7.1	7.1	6.8	
	N	25	25	24	25	
GD 6	MEAN	239	236	236	238	
	S.D.	8.7	8.5	7.8	6.7	
	N	25	25	24	25	
GD 9	MEAN	254	254	249	245*	
	S.D.	10.7	10.0	9.8	11.2	
	N	25	25	24	25	
GD 12	MEAN	269	269	267	254*	
	S.D.	18.9	11.6	10.3	13.0	
	N	25	25	24	25	
GD 15	MEAN	293	289	288	266*	
	S.D.	13.4	14.7	10.5	12.9	
	N	25	25	24	25	
GD 18	MEAN	322	319	316	292*	
	S.D.	15.9	17.7	15.3	17.9	
	N	25	25	24	25	
GD 20	MEAN	351	347	343	315*	
	S.D.	18.3	18.5	15.9	18.6	
	N	25	25	24	25	
PND 0	MEAN	274	273	267	244*	
	S.D.	13.2	19.0	14.2	12.2	
	N	25	25	24	25	
PND 4	MEAN	292	285	279*	256*	
	S.D.	14.2	21.7	13.2	12.8	
	N	25	25	24	25	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]The number of dams evaluated. One dam at 6 mg base/kg/day was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 200 (F_0 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 4-F (mg base/kg/day)
PND 7	MEAN	303	295	293	264*
	S.D.	16.8	18.5	13.9	11.2
	N[a]	25	25	24	25
PND 10	MEAN	315	309	302*	273*
	S.D.	20.1	21.8	14.4	12.4
	N	25	25	24	25
PND 14	MEAN	329	318	320	283*
	S.D.	25.3	24.8	18.8	16.0
	N	25	25	24	25
PND 17	MEAN	330	317*	317	289*
	S.D.	19.6	21.4	18.3	18.1
	N	25	25	24	25
PND 21	MEAN	317	304	310	294*
	S.D.	21.0	21.8	22.9	18.5
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]The number of dams evaluated. One dam at 6 mg base/kg/day was not pregnant.

Table 5

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)[a]

STUDY: 200 (F_0 Generation) SEX: FEMALE

PERIOD[b]	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
GD 9	MEAN	15	18	12	7*
	S.D.	8.8	7.8	7.8	7.6
	N[c]	25	25	24	25
GD 12	MEAN	15	15	18	9*
	S.D.	11.0	6.6	4.8	7.1
	N	25	25	24	25
GD 15	MEAN	24	21	21	12*
	S.D.	13.1	5.5	3.5	7.8
	N	25	25	24	25
GD 18	MEAN	28	29	28	26
	S.D.	10.4	6.4	7.7	9.3
	N	25	25	24	25
GD 20	MEAN	29	28	28	23
	S.D.	13.7	5.3	5.9	8.2
	N	25	25	24	25
PND 0	MEAN	-77	-74	-76	-71
	S.D.	12.3	9.9	12.1	10.7
	N	25	25	24	25
PND 4	MEAN	18	12	12	12
	S.D.	10.0	13.8	10.5	9.7
	N	25	25	24	25
PND 7	MEAN	10	11	14	9
	S.D.	9.9	11.0	8.4	9.2
	N	25	25	24	25
PND 10	MEAN	12	14	9	9
	S.D.	10.7	15.6	7.6	8.2
	N	25	25	24	25
PND 14	MEAN	14	9	18	10
	S.D.	10.7	14.2	10.9	9.5
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is GD6.
[c]The number of dams evaluated. One dam at 6 mg base/kg/day was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF WEIGHT GAINS (Grams)[a]

STUDY: 200 (F_0 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
PND 17	MEAN	2	-1	-3	5
	S.D.	18.1	10.8	9.3	14.0
	N[b]	25	25	24	25
PND 21	MEAN	-13	-12	-7	5*
	S.D.	17.6	14.1	11.8	11.8
	N	25	25	24	25
TOTAL GAIN	MEAN	78	69	74	56*
	S.D.	17.6	19.1	21.8	18.9
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]The number of dams evaluated. One dam at 6 mg base/kg/day was not pregnant.

Table 6

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)[a]

STUDY: 200 (F_0 Generation) SEX: FEMALE

PERIOD	DOSE: / GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
GD 9[b]	INTAKE (g)	20.4	20.3	18.7*	17.2*
	S.D.	2.45	2.16	1.98	2.87
	N[c]	25	25	24	25
GD 12	INTAKE (g)	22.2	22.2	21.5	17.2*
	S.D.	4.19	2.41	1.96	4.12
	N	25	25	24	25
GD 15	INTAKE (g)	23.8	22.9	22.3	16.5*
	S.D.	2.12	2.70	1.95	2.32
	N	25	25	24	25
GD 18	INTAKE (g)	24.6	24.6	22.8	18.6*
	S.D.	3.09	3.14	2.03	2.52
	N	25	25	24	25
GD 20	INTAKE (g)	23.9	24.1	22.7	17.8*
	S.D.	3.31	3.07	2.80	2.05
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals.
[b]Baseline is GD6.
[c]The number of dams evaluated. One dam at 6 mg base/kg/day was not pregnant.

Table 7

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_0 Generation: Summary of Reproductive Parameters

Dose Level (mg base/kg/day)	0	2	6	18
Total Number Females/Group	25	25	25	25
Total Number of Surviving Females	25	25	25	25
Total Number of Pregnant Females	25	25	24	25
Gestation Duration[a,b]	21.8 ± 0.4	21.8 ± 0.4	21.6 ± 0.5	21.6 ± 0.5
Number F_1 Litters on PND0	25	25	24	25
Number Viable Pups/Litter on PND0[a,b] Males Females	 6.3 ± 2.4 5.4 ± 2.2	 6.3 ± 2.4 5.4 ± 2.1	 6.6 ± 1.3 5.7 ± 1.7	 6.1 ± 1.6 6.2 ± 2.3
Number Stillborn Pups/Litter on PND0[a,c]	0.1 ± 0.03	0.1 ± 0.03	0.0 ± 0.20	0.1 ± 0.30

[a]Mean ± S.D.
[b]Statisticlly analyzed using the ANOVA/Dunnett's test ($p \leq 0.05$)
[c]Statistically analyzed using the Kruskal-Wallis/Mann-Whitney U test ($p \leq 0.05$)

Table 8.1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL SIGNS (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: MALE

DOSE:	0	2	6	18 (mg base/kg/day)
GROUP:	1-M	2-M	3-M	4-M
Scheduled Sacrifice	50	50	48	50
Dark Material Around Eyes	0	1	0	1
Dehydrated	0	1	0	1
Total Number of Animals[a]	50	50	48	50

[a]Two animals/sex/litter were evaluated during the postweaning period. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 8.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL SIGNS (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: FEMALE

DOSE:	0	2	6	18 (mg base/kg/day)
GROUP:	1-F	2-F	3-F	4-F
Scheduled Sacrifice	49	50	48	50
Dark Material Around Eyes	0	0	0	1
Dehydrated	1	1	2	0
Total Number of Animals[a]	49	50	48	50

[a]Two animals/sex/litter were evaluated during the postweaning period. There was only one F_1 female in one litter at 0 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 9.1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P (F_1 Generation) SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	2 2-M	6 3-M	18 (mg base/kg/day) 4-M
PND 0	MEAN	6.7	6.7	6.4	6.2*
	S.D.	0.50	0.49	0.53	0.46
	N[a]	25	24	24	25
PND 4	MEAN	11.0	10.9	10.2	9.4*
	S.D.	1.13	1.01	1.08	1.04
	N	25	25	24	25
PND 7	MEAN	17.3	17.2	16.3	14.4*
	S.D.	1.58	1.72	1.78	1.70
	N	25	25	24	25
PND 14	MEAN	35.6	35.0	34.0	28.6*
	S.D.	2.50	3.54	2.82	2.80
	N	25	25	24	25
PND 21	MEAN	55.5	54.6	53.6	46.6*
	S.D.	4.34	5.83	4.80	4.64
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]The number of litters evaluated during the preweaning period. The PND0 body weights were inadvertently not recorded for one litter at 2 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 9.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P (F_1 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
PND 0	MEAN	6.2	6.4	6.1	5.9*
	S.D.	0.43	0.49	0.46	0.43
	N[a]	25	24	24	25
PND 4	MEAN	10.2	10.4	9.7	8.9*
	S.D.	1.07	1.06	0.90	1.04
	N	25	25	24	25
PND 7	MEAN	16.3	16.2	15.4	13.7*
	S.D.	1.43	1.74	1.55	1.71
	N	25	25	24	25
PND 14	MEAN	34.0	33.3	32.5	27.3*
	S.D.	2.27	3.41	2.53	3.01
	N	25	25	24	25
PND 21	MEAN	52.8	51.7	51.0	44.4*
	S.D.	3.71	5.45	4.24	5.12
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]The number of litters evaluated during the preweaning period. The PND0 body weights were inadvertently not recorded for one litter at 2 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 10.1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)[a] (Preweaning Period)

STUDY: 200P (F_1 Generation) SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	2 2-M	6 3-M	18 (mg base/kg/day) 4-M
PND 4[b]	MEAN	4.3	4.2	3.8	3.2*
	S.D.	0.70	0.77	0.70	0.69
	N[c]	25	24	24	25
PND 7	MEAN	6.4	6.3	6.0	5.0*
	S.D.	0.72	0.89	0.81	0.81
	N	25	25	24	25
PND 14	MEAN	18.2	17.7	17.7	14.2*
	S.D.	1.39	2.16	1.37	1.57
	N	25	25	24	25
PND 21	MEAN	20.0	19.6	19.6	18.0*
	S.D.	2.26	2.99	2.30	2.20
	N	25	25	24	25
TOTAL GAIN	MEAN	48.9	47.9	47.2	40.5
	S.D.	3.97	5.71	4.44	4.31
	N	25	24	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]The number of litters evaluated during the preweaning period. The PND0 body weights were inadvertently not recorded for one litter at 2 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 10.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF WEIGHT GAINS (Grams)[a] (Preweaning Period)

STUDY: 200P (F_1 Generation) SEX: FEMALE

PERIOD	DOSE: / GROUP:	0 / 1-F	2 / 2-F	6 / 3-F	18 (mg base/kg/day) / 4-F
PND 4[b]	MEAN	4.0	4.0	3.6	3.0*
	S.D.	0.75	0.74	0.61	0.72
	N[c]	25	24	24	25
PND 7	MEAN	6.1	5.9	5.7	4.8*
	S.D.	0.60	0.88	0.77	0.81
	N	25	25	24	25
PND 14	MEAN	17.7	17.1	17.1	13.6*
	S.D.	1.33	2.00	1.34	1.73
	N	25	25	24	25
PND 21	MEAN	18.8	18.4	18.6	17.1
	S.D.	1.93	2.69	1.96	2.59
	N	25	25	24	25
TOTAL GAIN	MEAN	46.5	45.3	45.0	38.6
	S.D.	3.48	5.24	3.92	4.84
	N	25	24	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]The number of litters evaluated during the preweaning period. The PND0 body weights were inadvertently not recorded for one litter at 2 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 11.1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	2 2-M	6 3-M	18 (mg base/kg/day) 4-M
PND 28	MEAN	99	97	96	88*
	S.D.	7.3	8.1	8.3	7.4
	N[a]	50	50	48	50
PND 35	MEAN	157	155	153	144*
	S.D.	10.2	13.3	12.9	10.8
	N	50	50	48	50
PND 42	MEAN	218	219	214	203*
	S.D.	13.2	15.6	16.7	13.8
	N	50	50	48	50
PND 49	MEAN	282	285	282	266*
	S.D.	15.7	19.2	21.1	18.0
	N	50	50	48	50
PND 56	MEAN	338	343	338	321*
	S.D.	21.4	24.1	25.1	25.5
	N	50	50	48	50
PND 63	MEAN	386	389	386	371*
	S.D.	23.8	33.9	30.8	25.3
	N	50	50	48	50
PND 70	MEAN	426	430	427	410*
	S.D.	27.8	34.4	35.2	28.9
	N	50	50	48	50
PND 77	MEAN	457	454	453	433
	S.D.	32.7	32.6	35.2	36.6
	N[b]	25	25	24	25
PND 84	MEAN	490	488	485	466
	S.D.	35.2	35.1	36.9	39.3
	N	25	25	24	25
PND 91	MEAN	514	512	510	493
	S.D.	39.0	37.8	40.2	41.4
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Two animals/sex/litter were evaluated during the postweaning period on PND28 - 70.
[b]One animal/sex/litter was evaluated during the postweaning period on PND77 - 91 (i.e., during the fertility phase).

Note: There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 11.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: FEMALE

PERIOD	DOSE: / GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
PND 28	MEAN	90	90	88	80*
	S.D.	6.6	7.1	7.3	8.7
	N[a]	49	50	48	50
PND 35	MEAN	132	134	130	121*
	S.D.	9.2	8.8	10.3	12.0
	N	49	50	48	50
PND 42	MEAN	166	168	166	154*
	S.D.	11.8	10.6	12.6	14.6
	N	49	50	48	50
PND 49	MEAN	191	195	192	180*
	S.D.	14.9	11.9	15.7	16.9
	N	49	50	48	50
PND 56	MEAN	212	222*	211	205
	S.D.	16.8	14.8	23.2	20.4
	N	49	50	48	50
PND 63	MEAN	231	242*	234	226
	S.D.	19.2	16.4	22.5	23.4
	N	49	50	48	50
PND 70	MEAN	249	257	253	241
	S.D.	21.7	20.9	26.1	27.0
	N	49	50	48	50
PND 77	MEAN	288	297	283	276
	S.D.	23.5	17.6	25.5	25.3
	N[b]	25	25	24	25
PND 84	MEAN	324	334	317	314
	S.D.	25.7	23.4	27.3	23.6
	N	25	25	24	25
PND 91	MEAN	388	403	386	379
	S.D.	41.1	35.6	32.2	37.8
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Two animals/sex/litter were evaluated during the postweaning period on PND28 - 70. There was only one F_1 female in one litter at 0 mg base/kg/day.

[b]One animal/sex/litter was evaluated during the postweaning period on PND77 - 91 (i.e., during the fertility phase).

Note: There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 12.1

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF WEIGHT GAINS (Grams)[a] (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	2 2-M	6 3-M	18 (mg base/kg/day) 4-M
PND 35[b]	MEAN	58	57	58	56
	S.D.	4.3	8.2	5.9	4.3
	N[c]	50	50	48	50
PND 42	MEAN	61	64*	61	60
	S.D.	5.9	7.3	5.2	4.8
	N	50	50	48	50
PND 49	MEAN	64	66	67	62
	S.D.	6.0	6.9	6.6	7.2
	N	50	50	48	50
PND 56	MEAN	56	58	57	56
	S.D.	10.0	12.2	6.4	13.5
	N	50	50	48	50
PND 63	MEAN	48	46	48	50
	S.D.	6.6	16.7	9.5	9.2
	N	50	50	48	50
PND 70	MEAN	40	41	41	39
	S.D.	8.2	17.3	8.8	8.9
	N	50	50	48	50
TOTAL GAIN	MEAN	327	333	331	322
	S.D.	26.1	32.6	29.5	25.8
	N	50	50	48	50

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND28.
[c]Two animals/sex/litter were evaluated during the postweaning period from PND28 - 70. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 12.1 (contd.)

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF WEIGHT GAINS (Grams)[a] (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	2 2-M	6 3-M	18 (mg base/kg/day) 4-M
PND 77[b]	MEAN	28	31	26	25
	S.D.	7.6	12.9	6.7	7.6
	N[c]	25	25	24	25
PND 84	MEAN	33	34	32	32
	S.D.	6.5	6.5	7.1	6.3
	N	25	25	24	25
PND 91	MEAN	24	24	25	27
	S.D.	8.9	9.7	6.1	5.1
	N	25	25	24	25
TOTAL GAIN	MEAN	414	414	415	405
	S.D.	36.3	36.3	35.5	37.3
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND70.
[c]One animal/sex/litter was evaluated during the fertility phase of the postweaning period from PND70 - 91. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 12.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)[a] (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
PND 35[b]	MEAN	41	44*	42	41
	S.D.	5.3	4.2	5.4	5.3
	N[c]	49	50	48	50
PND 42	MEAN	34	34	36	33
	S.D.	6.6	5.0	5.7	6.1
	N	49	50	48	50
PND 49	MEAN	25	28	26	26
	S.D.	7.1	6.6	5.8	5.5
	N	49	50	48	50
PND 56	MEAN	21	26*	19	25
	S.D.	9.3	7.4	17.3	6.7
	N	49	50	48	50
PND 63	MEAN	19	20	23	21
	S.D.	7.4	5.3	16.0	6.1
	N	49	50	48	50
PND 70	MEAN	18	15	19	15
	S.D.	6.4	19.5	6.1	11.0
	N	49	50	48	50
TOTAL GAIN	MEAN	159	167	165	161
	S.D.	19.0	19.8	22.4	23.7
	N	49	50	48	50

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND28.
[c]Two animals/sex/litter were evaluated during the postweaning period from PND28 - 70. There was only one F_1 female in one litter at 0 mg base/kg/day. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 12.2

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF WEIGHT GAINS (Grams)[a] (Postweaning Period)

STUDY: 200L (F_1 Generation) SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	2 2-F	6 3-F	18 (mg base/kg/day) 4-F
PND 77[b]	MEAN	33	37	32	32
	S.D.	6.7	16.2	9.6	10.1
	N[c]	25	25	24	25
PND 84	MEAN	36	37	35	38
	S.D.	7.7	8.6	6.2	10.2
	N	25	25	24	25
PND 91	MEAN	64	69	69	65
	S.D.	28.4	23.8	17.1	26.6
	N	25	25	24	25
TOTAL GAIN	MEAN	297	313	299	300
	S.D.	39.2	35.5	28.1	35.3
	N	25	25	24	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period.
[b]Baseline is PND70.
[c]One animal/sex/litter was evaluated during the fertility phase of the postweaning period from PND70 - 91. There were 24 litters at 6 mg base/kg/day since one F_0 dam at this dose level was not pregnant.

Table 13

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Preweaning Survival[a]

Dose Level (mg base/kg/day)	0	2	6	18
Postnatal Day 0[b,c]				
Males	6.3 ± 2.4 (25)	6.3 ± 2.4 (25)	6.6 ± 1.3 (24)	6.1 ± 1.6 (25)
Females	5.4 ± 2.2 (25)	5.4 ± 2.1 (25)	5.7 ± 1.7 (24)	6.2 ± 2.3 (25)
Postnatal Day 4 (Precull)[b,c,d]				
Males	6.3 ± 2.3 (25)	6.3 ± 2.4 (25)	6.4 ± 1.2 (24)	5.9 ± 1.7 (25)
Females	5.4 ± 2.1 (25)	5.2 ± 2.0 (25)	5.6 ± 1.7 (24)	6.2 ± 2.3 (25)
Postnatal Day 7[b,c]				
Males	3.8 ± 0.5 (25)	3.9 ± 0.4 (25)	4.0 ± 0.0 (24)	3.9 ± 0.3 (25)
Females	3.7 ± 0.7 (25)	3.6 ± 0.7 (25)	3.8 ± 0.6 (24)	3.9 ± 0.5 (25)
Postnatal Day 14[b,c]				
Males	3.8 ± 0.5 (25)	3.9 ± 0.4 (25)	4.0 ± 0.0 (24)	3.9 ± 0.3 (25)
Females	3.7 ± 0.7 (25)	3.6 ± 0.7 (25)	3.8 ± 0.6 (24)	3.9 ± 0.5 (25)
Postnatal Day 21[b,c]				
Males	3.8 ± 0.5 (25)	3.9 ± 0.4 (25)	4.0 ± 0.0 (24)	3.9 ± 0.3 (25)
Females	3.7 ± 0.7 (25)	3.6 ± 0.7 (25)	3.8 ± 0.6 (24)	3.9 ± 0.5 (25)

[a]Statistically analyzed using the ANOVA/Dunnett's test ($p \leq 0.05$)
[b]Mean ± S.D. for the number of viable pups/litter
[c]Number in parenthesis = number of litters/group
[d]Litters were culled to 4/sex on PND4

Table 14

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Developmental Parameters[a]

Dose Level (mg base/kg/day)	0	2	6	18
Surface Righting Reflex[b,c]				
Males	2.0 ± 0.5 (25)	2.0 ± 0.6 (25)	2.0 ± 0.6 (24)	1.0 ± 0.6 (25)
Females	2.0 ± 0.6 (25)	2.0 ± 0.7 (25)	2.0 ± 0.6 (24)	2.0 ± 0.6 (25)
Incisor Appearances[b,c]				
Males	10.7 ± 0.9 (25)	10.4 ± 0.7 (25)	10.6 ± 0.7 (24)	10.7 ± 0.9 (25)
Females	10.5 ± 0.7 (25)	10.3 ± 0.7 (25)	10.5 ± 0.6 (24)	10.8 ± 0.8 (25)
Eyes Open[b,c]				
Males	14.2 ± 0.4 (25)	14.3 ± 0.4 (25)	14.4 ± 0.5 (24)	14.6 ± 0.5* (25)
Females	14.1 ± 0.4 (25)	14.1 ± 0.6 (25)	14.2 ± 0.5 (24)	14.5 ± 0.6* (25)
Cliff Avoidance[b,c]				
Males	15.0 ± 0.1 (25)	15.1 ± 0.1 (25)	15.1 ± 0.1 (24)	15.1 ± 0.2 (25)
Females	15.0 ± 0.0 (25)	15.0 ± 0.1 (25)	15.0 ± 0.1 (24)	15.0 ± 0.2 (25)
Preputial Separation[b,d]				
Males	38.9 ± 2.2 (50)	38.7 ± 1.9 (50)	39.7 ± 1.9 (48)	39.8 ± 2.5 (50)
Vaginal Opening[b,d]				
Females	32.4 ± 1.2 (49)	31.9 ± 1.4 (50)	32.1 ± 1.0 (48)	32.2 ± 1.2 (50)

[a]Statistically analyzed using the Kruskal-Wallis/Mann-Whitney U test ($p \leq 0.05$)
[b]Mean ± S.D. for day of attainment of the landmark (e.g., surface righting reflex was attained essentially on PND2)
[c]Number in parenthesis = number litters/group evaluated (These landmarks were observed in the preweaning period)
[d]Number in parenthesis = number animals/group evaluated (These landmarks were observed in the postweaning period)
*Statistically different from the control group

Table 15

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Functional Observational Battery[a]

Dose Level (mg base/kg/day)	0	2	6	18
Number of Males/Females[b]	50/49[c]	50/50	48/48[d]	50/50
Home Cage Observations (Posture/palpebral closure/convulsions/ vocalization/biting)				
Males	NE	NE	NE	NE
Females	NE	NE	NE	NE
Ease of Handling (During removal from cage/when held)				
Males	NE	NE	NE	NE
Females	NE	NE	NE	NE
General Appearance (Lacrimation/salivation/fur appearance)				
Males	NE	NE	NE	NE
Females	NE	NE	NE	NE
Open Field Activity (Sniffing/freezing/grooming/no. fecal boluses and urine spots/diarrhea)				
Males	NE	NE	NE	NE
Females	NE	NE	NE	NE
Reflexes (Acoustic/approach/touch/tail pinch/air righting)				
Males	NE	NE	NE	NE
Females	NE	NE	NE	NE
Physical Measures (Body weight/temperature)				
Males	NE	NE	NE	↓BW*
Females	NE	NE	NE	↓BW*

[a]Statistical analyses were performed using the ANOVA/Dunnett's test (count, interval, and rank data); the Kruskal-Wallis/Mann-Whitney U test (rank data), or the Chi-Square/Fischer's Exact test for rank (descriptive and quantal data) ($p \leq 0.05$)
[b]When possible, two animals/sex/litter were evaluated.
[c]There was only one female in litter No. 109.
[d]There were 24 litters in the 6 mg base/kg/day group (F_0 dam No. 159 was not pregnant).
NE = No effect for all parameters evaluated unless otherwise indicated.
↓BW = Decreased body weights
*Statistically different from the control group

Table 16

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Motor Activity[a]

Dose Level (mg base/kg/day)	0	2	6	18
Active Time in Horizontal Plane[b,c]				
Males	666.1 ± 104.02 (48)[d]	671.4 ± 116.88 (50)	637.1 ± 186.18 (48)[f]	654.3 ± 138.12 (50)
Females	659.6 ± 83.63 (49)[e]	669.3 ± 106.60 (50)	645.3 ± 166.91 (48)[f]	664.0 ± 139.83 (50)
Total Time in Center of Enclosure[b,c]				
Males	49.4 ± 37.84 (48)[d]	54.6 ± 45.97 (50)	94.6 ± 236.58 (48)[f]	74.4 ± 167.28 (50)
Females	76.6 ± 58.90 (49)[e]	58.7 ± 43.10 (50)	96.4 ± 235.75 (48)[f]	72.7 ± 166.08 (50)
Total Time Rearing[b,c]				
Males	293.9 ± 103.97 (48)[d]	319.8 ± 87.84 (50)	297.9 ± 94.27 (48)[f]	271.8 ± 98.63 (50)
Females	389.4 ± 111.68 (49)[e]	385.2 ± 122.61 (50)	340.3 ± 112.58 (48)[f]	332.2 ± 128.70* (50)

[a]Statistically analyzed using the ANOVA/Dunnett's test ($p \leq 0.05$)
[b]Mean ± S.D. for the number of seconds out of 1200 seconds (i.e., 20 minutes) the animals were actively moving (i.e, in the horizontal plane), active and/or resting in the center of the enclosure, or in a rearing posture (i.e., with the front paws off the floor).
[c]Number in parenthesis = number of animals/group tested. When possible, two animals/sex/litter were evaluated.
[d]The data for both males from litter No. 104 was recorded for the full 20 minutes. However, due to a technical error, the data could not be analyzed.
[e]There was only one female in litter No. 109.
[f]There were 24 litters in the 6 mg base/kg/day group (F_0 dam No. 159 was not pregnant).

Table 17

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Learning and Memory

Dose Level (mg base/kg/day)	0	2	6	18
Acquistion (Learning)[a]				
Males	25/25	24/25[d]	23/24[e,f]	25/25
Females	25/25	25/25	24/24[e]	25/25
Retention (Memory)[b,c]				
Males	159.4 ± 11.7	145.0 ± 11.0	147.5 ± 12.2	132.5 ± 13.5
Females	124.5 ± 13.7	132.5 ± 13.9	96.2 ± 12.9	137.2 ± 11.2

[a]The numbers of animals that achieved acquisition/number of animals tested.
[b]Mean ± S.D. for the number of seconds out of 180 seconds that the animals remained in the illuminated chamber of the enclosure (i.e., the number of seconds the animal demonstrated retention of the acquired behavior).
[c]Statistically analyzed using the Kruskal-Wallis/Dunnett's test ($p \leq 0.05$)
[d]One male (No. 14901) did not achieve acquisition (i.e., never crossed from the illuminated to the dark chamber of the enclosure). Consequently, this animal never received the negative reinforcement and could not be tested for retention.
[e]There were 24 litters in the 6 mg base/kg/day group (F_0 dam No. 159 was not pregnant).
[f]One male (No. 15101) did not achieve acquisition (i.e., never crossed from the illuminated to the dark chamber of the enclosure). Consequently, this animal never received the negative reinforcement and could not be tested for retention.

Table 18

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Summary of Reproductive Data

Dose Level (mg/base/kg/day)	0	2	6	18
Number of Mating Pairs	25	25	24[f]	25
Number of F_1 Females Pregnant	22	24	24	22
Gestation Duration[a,b]	21.4 ± 0.6	21.8 ± 0.5	21.5 ± 0.6	21.4 ± 0.5
Mating Index[c,d]	100% (25/25)	100% (25/25)	100% (24/24)	100% (25/25)
Fertility Index[c,d]	88%[g] (22/25)	96%[g] (24/25)	100% (24/24)	88%[g] (22/25)
Number Viable F_2 Pups[a,b]	15.4 ± 1.8	15.2 ± 2.3	14.7 ± 3.2	14.5 ± 2.2
Number Stillborn F_2 Pups[a,e]	0.3 ± 0.5	0.2 ± 0.6	0.1 ± 0.3	0.4 ± 0.6

[a]Mean ± S.D.
[b]Statistically analyzed by the ANOVA/Dunnett's test ($p \leq 0.05$)
[c]Statistically analyzed using the Chi-Square/Fisher's Exact test ($p \leq 0.05$)
[d]Mating Index = (No. with evidence of mating/No. cohoused) x 100
[d]Fertility Index = (No. pregnant/No. with evidence of mating) x 100
[e]Statistically analyzed using the Kruskal-Wallis/Mann-Whitney U test ($p \leq 0.05$)
[f]There were 24 litters in the 6 mg base/kg/day group (F_0 dam No. 159 was not pregnant).
[g]Three females at 0 mg base/kg/day, one female at 2 mg base/kg/day, and three females at 18 mg base/kg/day had evidence of mating (i.e., sperm in the vaginal washing), but were not pregnant when necropsied on GD25.

APPENDIX A

ANALYTICAL CHEMISTRY REPORT

DRAFT

Oral Prenatal and Postnatal Development Study of WR238605 Succinate In Rats
UIC/TRL Study Number 200

Part I: **Identity, Purity and Stability of Neat WR238605 Succinate**

Part II: **Dosing Formulations Analysis of WR238605 Succinate in 1% Methylcellulose/0.2% Tween 80**

Analysts: A. Karl Larsen, Jr.
Thomas Tolhurst

Study Site: Drug Disposition Research Laboratory
College of Pharmacy
University of Illinois at Chicago
Chicago, Illinois 60612

Sponsor: Toxicology Research Laboratory
University of Illinois at Chicago
Chicago, Illinois 60612

Report Prepared by: Thomas Tolhurst

Report Prepared: October 7, 1996

Approved: October 11, 1996
Eugene F. Woods
Drug Disposition Research Laboratory

Part 1: Identity, Purity and Stability of Neat WR238605 Succinate

Objective

The objective of this study was to confirm the identity and establish the purity and stability of neat WR238605 Succinate (Bottle No. BM 12562).

Identification

GC-MS System

Gas Chromatograph:	Hewlett-Packard Model 5890 Series II
Mass Selective Detector (MSD):	Hewlett-Packard Model 5970
Analytical Column:	30 m x 0.25 mm ID, DB-1 with a 3 micron film thickness
GC Parameters:	Injector temp. 250 °C, oven temp. 70 °C initial, 270 °C final, 15 °C/minute ramp, carrier gas - helium, flow rate 2 mL/minute, split ratio 10:1

Procedure

Subject sample (WR238605 succinate) was submitted by the Toxicology Research Laboratory, (TRL). The sample was dissolved in hexane:ethanol (4:1) to a concentration of 0.8 μg base/mL and a 2 μL aliquot was injected on the column. The MSD scanned from 40 amu to 475 amu at a rate of 1 scan per second.

Results

The mass spectrum indicates a molecular ion m/e 463 (M^+ free base) and m/e 405 [M^+ free base minus $(CH_2)_3\ NH_2$]. This pattern is consistent with the structural formula and corresponds to the finding by SRI International (see SRI International Report No. 469, May 9, 1994).

The mass spectrum of the WR238605 sample was previously reported (see Analytical Chemistry Report of UIC/TRL Study No. 097 and UIC/TRL Study No. 098 from August 19, 1993) and it is shown in Figure 1.

Purity/Stability

The subject sample (WR238605 Succinate) was supplied by the TRL and stored at 0 to 4 °C when not being analyzed.

Description

A fine pale yellow powder, no obvious odor.

HPLC System

Solvent Delivery:	Waters Model 6000A Pump
Injector:	Rheodyne 7125 with 20μL sample loop
Analytical Column:	Bondclone ODS, 10μ, 300 mm x 3.9 mm (Phenomenex)
Detector:	Kratos, Spectroflow 773 UV Detector, 268 nm
Integrator:	Perkin Elmer LCI-100 Integrator
Mobile Phase:	75% methanol: 25% deionized water containing 6.9 grams of sodium acetate and 9 mL of 85% o-phosphoric acid; flow rate 1.5 mL/min

Procedure

Five solutions of WR238605 were prepared as follows. Twenty-five mg of WR238605 was weighed into each of five 25 mL volumetric flasks. The samples were dissolved in and the volume brought to mark with mobile phase. A 20 μL aliquot of each solution was chromatographed at 268 nm for purity determination.

Calculation of Purity

Quantitations were based on the assumption of equal detector response per unit weight of all UV-absorbing components. Areas of WR238605 and other detectable components in the subject sample chromatograms were employed in the following equation to calculate the percentage of WR238605 present in the sample:

$$\%\text{PURITY} = (\text{area of WR238605/total area - mobile phase}) \times 100$$

Stability

The stability of neat WR238605 Succinate was assessed by comparing the percent purity of WR238605 samples submitted for analysis prior to and following completion of UIC/TRL Study Number 200. A change in purity greater than 10% was considered to represent a significant loss of potency.

Results

Typical chromatograms are shown in Figure 2. The subject samples were found to contain less than 1% of UV-absorbing impurities. The percent purity of the initial and terminal WR238605 samples were 99.98 $\pm$ 0.00% and 99.81 $\pm$ 0.03%, respectively, and the assay results are presented in Tables 1 and 2. No loss of potency was found to have occurred over the period during which UIC/TRL Study Number 200 was conducted.

Figure 1

Mass Spectrum of WR238605 Sample

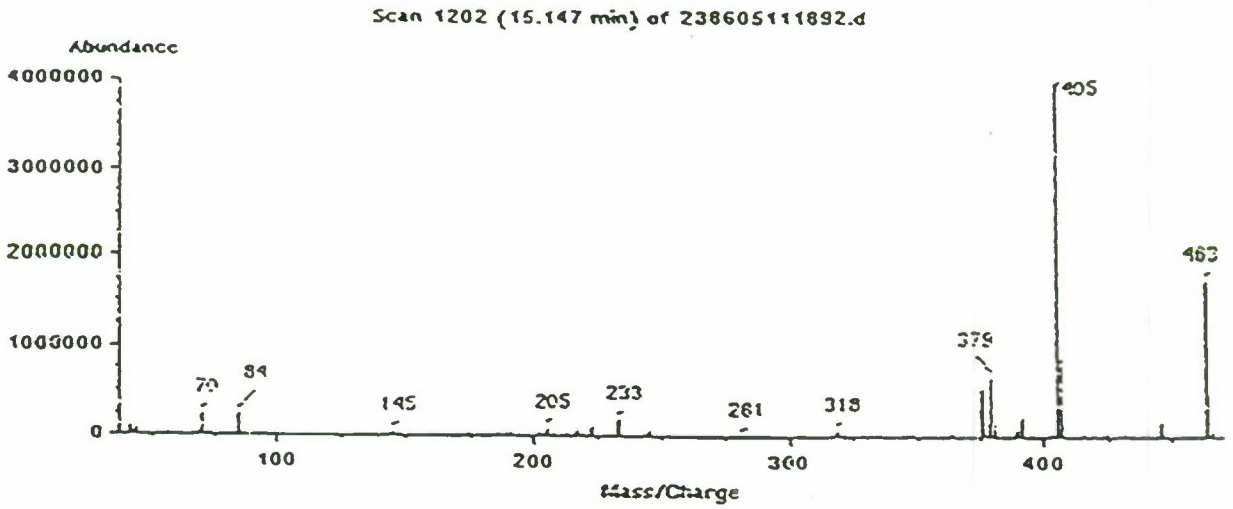
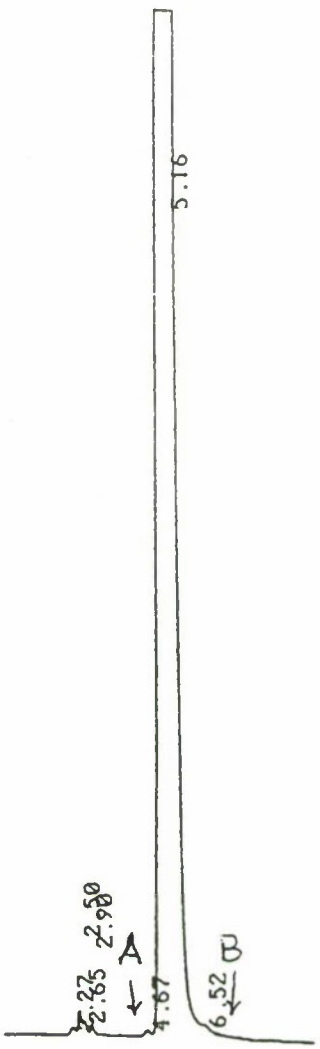
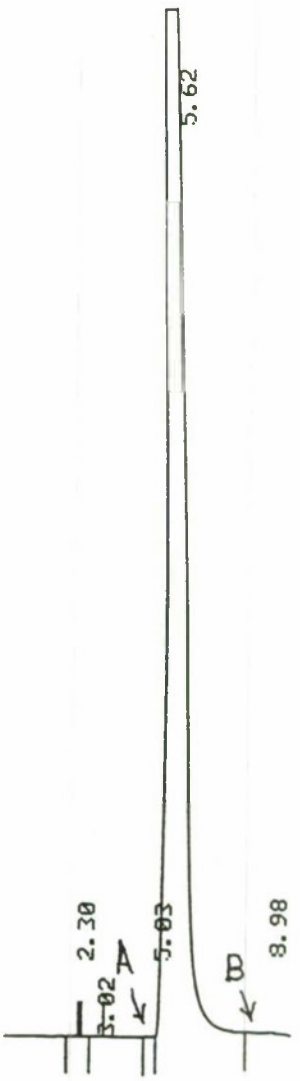


Figure 2

Chromatograms of WR238605 (Conc. 0.8 mg/mL, 268 nm)



Initial Sample



Terminal Sample

Table 1

Purity Data for WR238605 Succinate
Initial Sample

Solutions

Peak Identity	1	2	3	4	5
WR238605	48741020	48925026	50288590	50128658	50260853
A	1496	1474	____	____	2754
B	6938	7483	9422	8042	8896
% Purity*	99.98	99.98	99.98	99.98	99.98

*mean ± s.d. (99.98 ± 0.00)

Table 2

Purity Data for WR238605 Succinate Terminal Sample

	Solutions				
Peak Identity	1	2	3	4	5
WR238605	47249676	4735977	47125071	47058251	47534419
A	5073	4311	5717	5008	6589
B	77765	69101	79570	83397	103362
% Purity*	99.83	99.85	99.82	99.81	99.77

*mean ± s.d. (99.81 ± 0.03)

Part II: Dosing Formulations Analysis of WR238605 Succinate in 1% Methylcellulose/0.2% Tween 80

Introduction

Sample from UIC/TRL Study No. 200 were submitted by the TRL to the Drug Disposition Research Laboratory for the quantitation of WR238605 free base in dosing formulations. All samples submitted were analyzed by HPLC using the existing analytical method (SOP No. 01MA10-01).

Analytical Method

Regents

HPLC grade methanol, 85% o-phosphoric acid, and sodium acetate were purchased from Fisher Scientific. HPLC grade water was acquired through a Millipore, MILLI-Q Reagent Water System which was supplied with distilled water.

Standards

All WR238605 concentrations reflect free base value. A 0.8 mg base/mL WR238605 stock solution was prepared by weighing 100 mg of the drug (mole fraction = 0.8) into a 100 mL volumetric flask. The content was dissolved in and the volume brought to mark with mobile phase. A working calibration standard solution of 80μg base/mL was prepared by transferring 10.0 mL of the 0.80 mg base/mL stock solution to a 100 mL volumetric flask and diluting to mark with mobile phase. The remaining working calibration standards were prepared from the 80 μg base/mL WR238605 solution as follows:

Volume Transferred (mL)	Flask Volume (mL)	Final Concentration (μg base/mL)
1.0	10	8
2.0	10	16
4.0	10	32
6.0	10	48
8.0	10	64

Controls

Control A (0.8 mg base/mL) and control B (2.4 mg base/mL) were prepared by weighing 25 mg and 75 mg, respectively, of WR238605 Succinate salt into two 25 mL volumetric flasks. The contents were dissolved in and diluted to mark with mobile phase. Control A was further diluted 1:25 and Contol B was diluted 1:62.5 prior to analysis.

Sample Preparation

Triplicate dilutions of each suspension were prepared in mobile phase prior to HPLC analysis. The vehicle and the 0.4 mg base/mL suspension were diluted 1:10, and the 1.2 mg base/mL and the 3.6 mg base/mL suspension were diluted 1:25 and 1:100, respectively.

HPLC System

See part I: HPLC System

Calculations

A standard curve was run at the beginning and end of each assay day. Final concentrations for controls and samples were determined using a composite standard curve. The composite standard curve was determined by linear least squared regression analysis of the peak areas for WR238605 free base as a function of concentration. WR238605 concentrations (mg base/mL) for controls and samples were determined using the following equation:

$$\text{WR238605 Conc.} = (Y-B)/M \times (\text{d.f.}/1000)$$

Y = peak height

B = Y-intercept from composite standard curve

M = slope from composite standard curve

d.f. = dilution factor

The standard curves were linear over the range of WR238605 assayed (8 μg base/mL - 80 μg base/mL) and had correlation coefficients greater than 0.998. A representative standard curve is shown in Figure 3.

Results

Results of dosing formulations analysis for UIC/TRL Study No. 200 are presented in Table 3. All test article dosage formulations were within 10% of their respective target concentrations both prior to and after dosing.

Figure 3

Standard Curve of WR238606

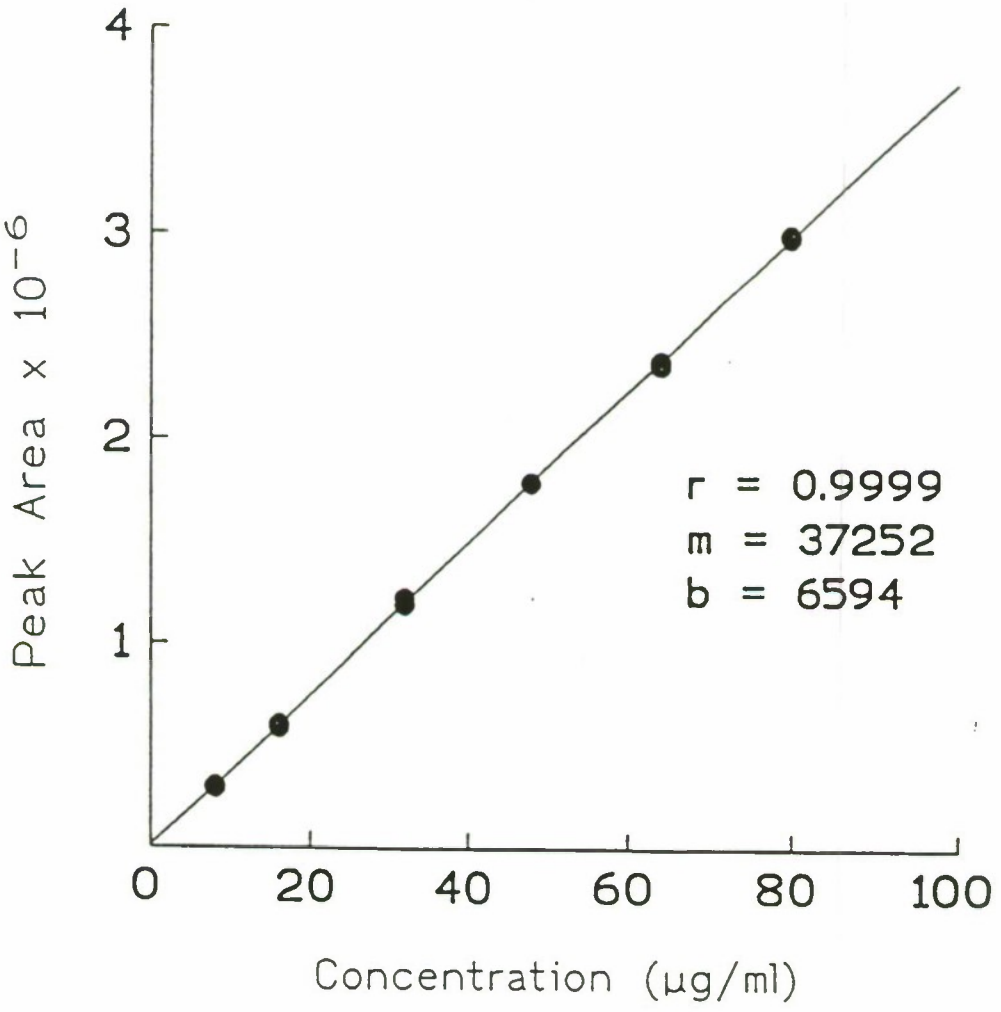


Table 3
Results of Dosing Formulations Analysis for
UIC/TRL Study Number 200

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
1	0.0	04/25/96	0	-	05/02/96	0	-
	0.4		0.398 ± 0.003	99.5		0.402 ± 0.003	101.0
	1.2		1.135 ± 0.048	94.6		1.178 ± 0.004	103.8
	3.6		3.618 ± 0.047	100.5		3.659 ± 0.045	101.1
2	0.0	05/02/96	0	-	05/09/96	0	-
	0.4		0.398 ± 0.002	99.5		0.397 ± 0.002	99.7
	1.2		1.188 ± 0.010	99.0		1.195 ± 0.004	100.6
	3.6		3.703 ± 0.010	102.9		3.730 ± 0.026	100.7
3	0.0	05/09/96	0	-	05/16/96	0	-
	0.4		0.396 ± 0.003	99.0		0.391 ± 0.003	98.7
	1.2		1.213 ± 0.010	101.1		1.186 ± 0.005	97.8
	3.6		3.684 ± 0.047	102.3		3.702 ± 0.020	100.5
4	0.0	05/16/96	0	-	05/23/96	0	-
	0.4		0.403 ± 0.004	100.8		0.425 ± 0.027	105.5
	1.2		1.219 ± 0.010	101.6		1.212 ± 0.006	99.4
	3.6		3.603 ± 0.154	100.1		3.745 ± 0.056	103.9
5	0.0	05/23/96	0	-	05/30/96	0	-
	0.4		0.420 ± 0.021	105.0		0.394 ± 0.004	93.8
	1.2		1.209 ± 0.022	100.8		1.211 ± 0.018	100.2
	3.6		3.662 ± 0.021	101.7		3.621 ± 0.075	98.9
6	0.0	05/30/96	0	-	06/06/96	0	-
	0.4		0.396 ± 0.004	99.0		0.408 ± 0.006	103.0
	1.2		1.223 ± 0.011	101.9		1.190 ± 0.010	97.3
	3.6		3.719 ± 0.041	103.3		3.675 ± 0.055	98.8
7	0.0	06/06/96	0	-	06/13/96	0	-
	0.4		0.400 ± 0.003	100.0		0.401 ± 0.002	100.3
	1.2		1.200 ± 0.030	100.0		1.210 ± 0.017	100.8
	3.6		3.629 ± 0.188	100.8		3.634 ± 0.188	100.1
8	0.0	06/13/96	0	-	06/20/96	0	-
	0.4		0.407 ± 0.003	101.8		0.394 ± 0.005	96.8
	1.2		1.149 ± 0.039	95.8		1.144 ± 0.029	99.6
	3.6		3.646 ± 0.131	101.3		3.714 ± 0.031	101.9

APPENDIX B

INDIVIDUAL F_0 GENERATION OBSERVATIONS (Clinical Signs)

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 1-F SEX: FEMALE
GD 6-PND 21 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
101	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
102	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
103	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
104	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
105	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
106	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
107	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
108	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
109	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
110	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
111	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
112	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
113	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 1-F SEX: FEMALE
GD 6-PND 21 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
114	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
115	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
116	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
117	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
118	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
119	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
120	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
121	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
122	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
123	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
124	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
125	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 2-F SEX: FEMALE
GD 6-PND 21 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
126	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
127	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
128	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
129	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
130	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
131	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
132	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
133	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
134	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
135	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
136	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
137	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
138	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 2-F SEX: FEMALE
GD 6-PND 21 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
139	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
140	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
141	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
142	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
143	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
144	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
145	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
146	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
147	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
148	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
149	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
150	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 3-F SEX: FEMALE
GD 6-PND 21 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
151	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
152	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
153	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
154	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
155	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
156	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
157	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
158	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
159	Normal Sacrificed[a]			GD 6-PND 3 GD 25
160	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
161	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
162	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
163	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

[a] F_0 dam No. 159 was not pregnant and was sacrificed on GD25.

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 3-F SEX: FEMALE
GD 6-PND 21 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
164	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
165	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
166	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
167	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
168	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
169	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
170	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
171	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
172	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
173	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
174	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
175	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 4-F SEX: FEMALE
GD 6-PND 21 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
176	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
177	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
178	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
179	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
180	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
181	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
182	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
183	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
184	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
185	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
186	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
187	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
188	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 200 GROUP: 4-F SEX: FEMALE
GD 6-PND 21 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
189	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
190	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
191	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
192	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
193	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
194	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
195	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
196	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
197	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
198	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
199	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21
200	Normal Scheduled Sacrifice			GD 6-PND 20 PND 21

DRAFT

SUMMARY OF OBSERVATION INCIDENCE

STUDY: 200 SEX: FEMALE

PERIOD	DOSE: (mg base/kg/day) GROUP:	0 1-F	2 2-F	6 3-F	18 4-F
GD 6					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 7					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 8					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 9					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 10					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 11					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 12					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 13					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 14					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 15					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF OBSERVATION INCIDENCE

STUDY: 200 SEX: FEMALE

PERIOD	DOSE: (mg base/kg/day) GROUP:	0 1-F	2 2-F	6 3-F	18 4-F
GD 16					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 17					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 18					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 19					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 20					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
GD 21					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
PND 0					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
PND 1					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
PND 2					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
PND 3					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

DRAFT

SUMMARY OF OBSERVATION INCIDENCE

STUDY: 200 SEX: FEMALE

PERIOD	DOSE: (mg base/kg/day) GROUP:	0 1-F	2 2-F	6 3-F	18 4-F
PND 4					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	24 96%	25 100%
Sacrificed [a]		0	0	1 4%	0
PND 5					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 6					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 7					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 8					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 9					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 10					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 11					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 12					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%
PND 13					
No. Observed		25	25	24	25
Normal		25 100%	25 100%	24 100%	25 100%

[a] F_0 dam No. 159 at 6 mg base/kg/day was not pregnant and was sacrificed on GD 25 (GD25 for this dam corresponded with PND4 for the group).

SUMMARY OF OBSERVATION INCIDENCE

STUDY: 200 SEX: FEMALE

PERIOD	DOSE: (mg base/kg/day) GROUP:	0 1-F	2 2-F	6 3-F	18 4-F
GD 14					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 15					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 16					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 17					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 18					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 19					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 20					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
GD 21					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

APPENDIX C

INDIVIDUAL F_0 GENERATION BODY WEIGHTS AND WEIGHT GAIN

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	GD 0	GD 5	GD 6	GD 9	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10
101	203	233	242	258	273	298	324	343	286	283	298	313
102	202	233	244	258	274	299	338	355	283	295	308	318
103	206	246	251	269	290	316	352	382	293	326	338	369
104	207	238	250	229	198	281	318	319	271	306	324	325
105	195	227	234	243	261	282	315	331	266	276	293	297
106	195	220	230	240	255	280	309	329	256	277	297	296
107	201	234	246	258	270	294	324	339	284	287	310	314
108	204	234	239	251	264	275	299	327	254	274	285	290
109	194	219	227	246	257	274	299	327	260	287	288	297
110	205	246	252	270	293	308	333	372	290	307	308	318
111	197	221	228	243	262	289	315	348	270	275	282	291
112	196	227	230	243	263	280	307	344	254	288	287	287
113	199	229	232	247	264	279	303	336	258	283	287	297
114	204	240	240	269	281	308	292	371	277	298	315	332
115	201	240	244	260	281	307	336	376	289	303	320	338
116	199	246	245	267	288	311	332	354	284	303	329	333
117	199	230	228	246	260	280	309	338	259	278	277	291
118	198	227	224	246	256	281	315	349	263	296	277	321
119	204	233	234	258	273	304	338	369	282	303	312	328
120	208	241	250	267	292	313	348	375	293	309	319	331
121	190	236	246	258	258	281	316	343	264	278	298	293
122	205	234	243	257	277	296	325	351	280	286	295	315
123	210	231	239	258	279	298	329	361	278	294	313	337
124	200	229	231	248	273	293	329	369	269	282	293	312
125	208	239	250	263	281	308	341	373	291	318	318	329
MEAN	201	233	239	254	269	293	322	351	274	292	303	315
S.D.	5.0	7.6	8.7	10.7	18.9	13.4	15.9	18.3	13.2	14.2	16.8	20.1
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 14	PND 17	PND 21
101	331	332	326
102	319	334	312
103	381	360	353
104	334	345	315
105	305	319	297
106	301	301	300
107	327	316	315
108	297	307	288
109	295	302	308
110	332	335	322
111	293	358	277
112	287	308	294
113	291	307	293
114	350	361	339
115	352	341	339
116	355	353	340
117	309	302	302
118	344	330	324
119	345	335	328
120	356	346	345
121	333	333	301
122	333	323	326
123	352	346	351
124	343	312	302
125	351	351	338
MEAN	329	330	317
S.D.	25.3	19.6	21.0
N	25	25	25

--: Data Unavailable

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	GD 0	GD 5	GD 6	GD 9	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10
126	204	234	221	264	282	308	338	363	301	312	325	327
127	203	239	249	263	282	311	358	392	303	303	322	321
128	205	234	243	256	267	288	317	335	269	272	280	294
129	205	233	243	249	275	302	328	352	279	286	299	309
130	199	229	233	249	267	293	330	356	272	286	294	310
131	194	222	229	241	257	280	318	345	264	262	287	294
132	200	237	239	257	276	292	310	339	275	308	312	318
133	204	234	237	248	260	283	305	340	264	286	285	288
134	195	217	222	233	250	263	290	319	243	214	251	262
135	198	229	230	244	261	271	293	323	257	273	282	291
136	194	223	228	241	262	277	301	328	250	273	281	284
137	196	227	230	246	260	280	308	341	250	276	278	282
138	206	240	243	254	267	285	311	347	264	285	284	286
139	203	241	238	264	272	295	321	346	273	286	301	311
140	194	229	222	246	258	283	309	343	275	270	288	303
141	200	245	244	269	284	313	352	375	298	318	318	337
142	200	233	232	257	266	290	318	349	275	287	292	337
143	200	239	234	264	271	295	318	347	278	289	303	323
144	200	230	231	248	258	281	313	351	254	290	297	311
145	210	239	245	265	288	303	329	359	303	308	311	324
146	201	237	243	261	283	300	332	361	301	302	285	341
147	209	236	241	253	268	288	316	346	268	274	285	341
148	201	232	239	254	248	260	291	309	242	261	285	289
149	209	245	252	271	291	315	347	377	297	312	338	341
150	199	223	228	241	261	274	310	330	258	288	302	309
MEAN	201	233	236	254	269	289	319	347	273	285	295	309
S.D.	4.7	7.1	8.5	10.0	11.6	14.7	17.7	18.5	19.0	21.7	18.5	21.8
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 14	PND 17	PND 21
126	336	345	322
127	328	339	316
128	304	305	308
129	313	319	306
130	311	314	289
131	308	308	302
132	326	332	298
133	292	302	290
134	274	268	268
135	286	306	276
136	287	292	278
137	290	291	251
138	298	310	292
139	326	312	314
140	316	321	301
141	340	316	317
142	321	321	315
143	341	331	332
144	326	321	319
145	336	318	326
146	380	372	335
147	305	292	297
148	315	314	318
149	369	352	344
150	325	316	298
MEAN	318	317	304
S.D.	24.8	21.4	21.8
N	25	25	25

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	GD 0	GD 5	GD 6	GD 9	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10
151	204	244	252	262	281	305	340	358	295	298	325	332
152	194	220	228	250	265	290	325	352	273	291	298	305
153	204	227	232	245	263	285	315	327	261	273	294	306
154	200	232	237	239	261	280	314	333	250	269	277	281
155	206	234	242	247	267	291	321	344	260	271	278	289
156	206	239	244	237	261	288	323	349	266	273	288	294
157	193	226	228	234	253	279	300	332	252	275	287	297
158	192	218	220	236	251	271	302	336	256	261	277	280
159[a]	--	--	--	--	--	--	--	--	--	--	--	--
160	207	237	241	241	260	279	305	336	257	270	273	286
161	202	230	232	243	261	282	311	342	266	283	283	285
162	209	240	243	256	266	283	301	332	266	285	300	307
163	205	235	238	249	266	287	315	346	249	285	284	303
164	205	239	235	252	268	286	309	338	275	278	292	309
165	202	233	233	242	259	283	302	336	267	271	305	304
166	208	242	238	253	263	283	297	323	256	271	289	300
167	200	232	230	244	261	286	312	335	271	271	291	298
168	208	245	241	266	279	307	330	370	289	292	303	316
169	200	228	221	239	252	272	285	308	261	256	280	292
170	202	230	230	246	260	278	306	335	240	270	283	289
171	200	227	235	242	270	295	320	348	282	282	303	327
172	206	234	242	250	279	293	330	357	266	278	285	300
173	208	239	239	262	284	304	326	357	287	300	311	321
174	206	242	248	268	288	308	348	374	284	314	322	310
175	204	237	241	262	281	299	341	372	285	289	304	325
MEAN	203	234	236	249	267	288	316	343	267	279	293	302
S.D.	4.7	7.1	7.8	9.8	10.3	10.5	15.3	15.9	14.2	13.2	13.9	14.4
N	24	24	24	24	24	24	24	24	24	24	24	24

--: Data Unavailable

[a] F_0 dam No. 159 was not pregnant.

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 14	PND 17	PND 21
151	353	347	342
152	326	314	310
153	307	316	294
154	299	287	288
155	298	299	275
156	298	304	287
157	312	318	302
158	304	285	284
159[a]	--	--	--
160	292	296	292
161	296	297	279
162	310	311	273
163	329	315	319
164	331	325	333
165	332	339	333
166	315	330	317
167	321	321	314
168	331	337	326
169	303	297	293
170	321	315	327
171	342	342	334
172	325	308	318
173	353	336	329
174	355	344	353
175	327	329	326
MEAN	320	317	310
S.D.	18.8	18.3	22.9
N	24	24	24

--: Data Unavailable

[a] F_0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	GD 0	GD 5	GD 6	GD 9	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10
176	195	232	244	250	249	241	270	287	231	246	269	267
177	208	226	236	246	254	261	290	298	236	239	258	255
178	200	239	250	269	286	290	328	337	260	278	284	281
179	200	229	236	240	241	260	281	297	233	249	257	277
180	205	236	244	259	264	275	294	300	233	243	259	265
181	200	234	243	240	239	260	272	298	238	243	266	261
182	204	246	246	245	237	263	286	317	243	265	255	269
183	204	231	237	249	260	277	315	341	252	280	282	293
184	200	229	235	246	263	279	296	330	236	264	252	267
185	192	223	227	239	251	256	280	309	235	254	266	270
186	192	217	223	228	241	243	250	280	226	234	242	253
187	204	236	242	254	263	267	283	310	237	259	268	281
188	195	230	229	229	243	249	281	309	231	257	273	281
189	206	229	232	229	236	254	270	303	240	236	238	252
190	206	234	232	222	243	260	286	310	237	257	272	277
191	199	242	236	247	260	272	303	328	263	267	278	294
192	202	245	242	243	257	271	292	310	245	252	256	269
193	201	237	235	241	247	274	309	341	258	262	275	286
194	208	235	241	253	253	266	311	342	255	264	267	287
195	200	237	243	262	278	291	310	345	265	263	266	293
196	203	236	241	256	263	269	305	324	259	260	259	275
197	210	238	239	251	264	277	300	323	250	252	267	271
198	210	242	247	252	264	273	309	325	263	272	276	285
199	209	232	238	234	236	251	271	290	228	236	259	258
200	203	226	229	242	257	272	304	325	240	264	267	269
MEAN	202	234	238	245	254	266	292	315	244	256	264	273
S.D.	5.1	6.8	6.7	11.2	13.0	12.9	17.9	18.6	12.2	12.8	11.2	12.4
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 200 GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 14	PND 17	PND 21
176	276	279	275
177	275	287	292
178	273	290	279
179	284	295	301
180	255	266	271
181	272	280	291
182	284	306	282
183	310	311	310
184	269	298	291
185	270	292	274
186	254	252	261
187	281	273	290
188	300	301	306
189	257	260	267
190	281	293	307
191	304	321	326
192	283	292	301
193	295	249	263
194	296	293	313
195	307	308	321
196	287	295	308
197	292	287	313
198	298	307	301
199	273	278	294
200	303	302	312
MEAN	283	289	294
S.D.	16.0	18.1	18.5
N	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10	PND 14	PND 17
101	16	15	25	26	19	-57	-3	15	15	18	1
102	14	16	25	39	17	-72	12	13	10	1	15
103	18	21	26	36	30	-89	33	12	31	12	-21
104	-21	-31	83	37	1	-48	35	18	1	9	11
105	9	18	21	33	16	-65	10	17	4	8	14
106	10	15	25	29	20	-73	21	20	-1	5	0
107	12	12	24	30	15	-55	3	23	4	13	-11
108	12	13	11	24	28	-73	20	11	5	7	10
109	19	11	17	25	28	-67	27	1	9	-2	7
110	18	23	15	25	39	-82	17	1	10	14	3
111	15	19	27	26	33	-78	5	7	9	2	65
112	13	20	17	27	37	-90	34	-1	0	0	21
113	15	17	15	24	33	-78	25	4	10	-6	16
114	29	12	27	-16	79	-94	21	17	17	18	11
115	16	21	26	29	40	-87	14	17	18	14	-11
116	22	21	23	21	22	-70	19	26	4	22	-2
117	18	14	20	29	29	-79	19	-1	14	18	-7
118	22	10	25	34	34	-86	33	-19	44	23	-14
119	24	15	31	34	31	-87	21	9	16	17	-10
120	17	25	21	35	27	-82	16	10	12	25	-10
121	12	D	23	35	27	-79	14	20	-5	40	0
122	14	20	19	29	26	-71	6	9	20	18	-10
123	19	21	19	31	32	-83	16	19	24	15	-6
124	17	25	20	36	40	-100	13	11	19	31	-31
125	13	18	27	33	32	-82	27	0	11	22	0
MEAN	15	15	24	28	29	-77	18	10	12	14	2
S.D.	8.8	11.0	13.1	10.4	13.7	12.3	10.0	9.9	10.7	10.7	18.1
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is GD6.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 21	TOTAL GAIN
101	-6	84
102	-22	68
103	-7	102
104	-30	65
105	-22	63
106	-1	70
107	-1	69
108	-19	49
109	6	81
110	-13	70
111	-81	49
112	-14	64
113	-14	61
114	-22	99
115	-2	95
116	-13	95
117	0	74
118	-6	100
119	-7	94
120	-1	95
121	-32	55
122	3	83
123	5	112
124	-10	71
125	-13	88
MEAN	-13	78
S.D.	17.6	17.6
N	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10	PND 14	PND 17
126	43	18	26	30	25	-62	11	13	2	9	9
127	14	19	29	47	34	-89	0	19	-1	7	11
128	13	11	21	29	18	-66	3	8	14	10	1
129	6	26	27	26	24	-73	7	13	10	4	6
130	16	18	26	37	26	-84	14	8	16	1	3
131	12	16	23	38	27	-81	-2	25	7	14	0
132	18	19	16	18	29	-64	33	4	6	8	6
133	11	12	23	22	35	-76	22	-1	3	4	10
134	11	17	13	27	29	-76	-29	37	11	12	-6
135	14	17	10	22	30	-66	16	9	9	-5	20
136	13	21	15	24	27	-78	23	8	3	3	5
137	16	14	20	28	33	-91	26	2	4	8	1
138	11	13	18	26	36	-83	21	-1	2	12	12
139	26	8	23	26	25	-73	13	15	10	15	-14
140	24	12	25	26	34	-68	-5	18	15	13	5
141	25	15	29	39	23	-77	20	0	19	3	-24
142	25	9	24	28	31	-74	12	5	45	-16	0
143	30	7	24	23	29	-69	11	14	20	18	-10
144	17	10	23	32	38	-97	36	7	14	15	-5
145	20	23	15	26	30	-56	5	3	13	12	-18
146	18	22	17	32	29	-60	1	-17	56	39	-8
147	12	15	20	28	30	-78	6	11	56	-36	-13
148	15	-6	12	31	18	-67	19	24	4	26	-1
149	19	20	24	32	30	-80	15	26	3	28	-17
150	13	20	13	36	20	-72	30	14	7	16	-9
MEAN	18	15	21	29	28	-74	12	11	14	9	-1
S.D.	7.8	6.6	5.5	6.4	5.3	9.9	13.8	11.0	15.6	14.2	10.8
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is GD6.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 21	TOTAL GAIN
126	-23	101
127	-23	67
128	3	65
129	-13	63
130	-25	56
131	-6	73
132	-34	59
133	-12	53
134	0	46
135	-30	46
136	-14	50
137	-40	21
138	-18	49
139	2	76
140	-20	79
141	1	73
142	-6	83
143	1	98
144	-2	88
145	8	81
146	-37	92
147	5	56
148	4	79
149	-8	92
150	-18	70
MEAN	-12	69
S.D.	14.1	19.1
N	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10	PND 14	PND 17
151	10	19	24	35	18	-63	3	27	7	21	-6
152	22	15	25	35	27	-79	18	7	7	21	-12
153	13	18	22	30	12	-66	12	21	12	1	9
154	2	22	19	34	19	-83	19	8	4	18	-12
155	5	20	24	30	23	-84	11	7	11	9	1
156	-7	24	27	35	26	-83	7	15	6	4	6
157	6	19	26	21	32	-80	23	12	10	15	6
158	16	15	20	31	34	-80	5	16	3	24	-19
159[c]	--	--	--	--	--	--	--	--	--	--	--
160	0	19	19	26	31	-79	13	3	13	6	4
161	11	18	21	29	31	-76	17	0	2	11	1
162	13	10	17	18	31	-66	19	15	7	3	1
163	11	17	21	28	31	-97	36	-1	19	26	-14
164	17	16	18	23	29	-63	3	14	17	22	-6
165	9	17	24	19	34	-69	4	34	-1	28	7
166	15	10	20	14	26	-67	15	18	11	15	15
167	14	17	25	26	23	-64	0	20	7	23	0
168	25	13	28	23	40	-81	3	11	13	15	6
169	18	13	20	13	23	-47	-5	24	12	11	-6
170	16	14	18	28	29	-95	30	13	6	32	-6
171	7	28	25	25	28	-66	0	21	24	15	0
172	8	29	14	37	27	-91	12	7	15	25	-17
173	23	22	20	22	31	-70	13	11	10	32	-17
174	20	20	20	40	26	-90	30	8	-12	45	-11
175	21	19	18	42	31	-87	4	15	21	2	2
MEAN	12	18	21	28	28	-76	12	14	9	18	-3
S.D.	7.8	4.8	3.5	7.7	5.9	12.1	10.5	8.4	7.6	10.9	9.3
N	24	24	24	24	24	24	24	24	24	24	24

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is GD6.
[c]F_0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 21	TOTAL GAIN
151	-5	90
152	-4	82
153	-22	62
154	1	51
155	-24	33
156	-17	43
157	-16	74
158	-1	64
159[c]	--	--
160	-4	51
161	-18	47
162	-38	30
163	4	81
164	8	98
165	-6	100
166	-13	79
167	-7	84
168	-11	85
169	-4	72
170	12	97
171	-8	99
172	10	76
173	-7	90
174	9	105
175	-3	85
MEAN	-7	74
S.D.	11.8	21.8
N	24	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]F_0 dam No. 159 was not pregnant.

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20	PND 0	PND 4	PND 7	PND 10	PND 14	PND 17
176	6	-1	-8	29	17	-56	15	23	-2	9	3
177	10	8	7	29	8	-62	3	19	-3	20	12
178	19	17	4	38	9	-77	18	6	-3	-8	17
179	4	1	19	21	16	-64	16	8	20	7	11
180	15	5	11	19	6	-67	10	16	6	-10	11
181	-3	-1	21	12	26	-60	5	23	-5	11	8
182	-1	-8	26	23	31	-74	22	-10	14	15	22
183	12	11	17	38	26	-89	28	2	11	17	1
184	11	17	16	17	34	-94	28	-12	15	2	29
185	12	12	5	24	29	-74	19	12	4	0	22
186	5	13	2	7	30	-54	8	8	11	1	-2
187	12	9	4	16	27	-73	22	9	13	0	-8
188	0	14	6	32	28	-78	26	16	8	19	1
189	-3	7	18	16	33	-63	-4	2	14	5	3
190	-10	21	17	26	24	-73	20	15	5	4	12
191	11	13	12	31	25	-65	4	11	16	10	17
192	1	14	14	21	18	-65	7	4	13	14	9
193	6	6	27	35	32	-83	4	13	11	9	-46
194	12	0	13	45	31	-87	9	3	20	9	-3
195	19	16	13	19	35	-80	-2	3	27	14	1
196	15	7	6	36	19	-65	1	-1	16	12	8
197	12	13	13	23	23	-73	2	15	4	21	-5
198	5	12	9	36	16	-62	9	4	9	13	9
199	-4	2	15	20	19	-62	8	23	-1	15	5
200	13	15	15	32	21	-85	24	3	2	34	-1
MEAN	7	9	12	26	23	-71	12	9	9	10	5
S.D.	7.6	7.1	7.8	9.3	8.2	10.7	9.7	9.2	8.2	9.5	14.0
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is GD6.

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 200 GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 21	TOTAL GAIN
176	-4	31
177	5	56
178	-11	29
179	6	65
180	5	27
181	11	48
182	-24	36
183	-1	73
184	-7	56
185	-18	47
186	9	38
187	17	48
188	5	77
189	7	35
190	14	75
191	5	90
192	9	59
193	14	28
194	20	72
195	13	78
196	13	67
197	26	74
198	-6	54
199	16	56
200	10	83
MEAN	5	56
S.D.	11.8	18.9
N	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.

APPENDIX D

INDIVIDUAL F_0 GENERATION FOOD CONSUMPTION

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 200 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20
101	21.7	24.0	23.0	20.3	25.5
102	21.0	24.3	23.0	24.7	23.5
103	21.3	24.3	22.3	23.0	25.0
104	15.0	5.3	25.0	23.3	24.0
105	19.3	21.7	22.7	18.7	26.0
106	17.7	20.3	20.3	22.3	22.5
107	22.0	23.3	23.7	24.3	27.0
108	19.0	19.3	21.7	19.3	19.5
109	19.3	20.7	20.0	24.3	24.5
110	23.3	24.7	26.0	26.7	25.5
111	19.0	22.3	22.7	27.0	24.5
112	18.3	19.3	19.7	32.7	30.5
113	20.0	19.7	24.7	26.7	22.5
114	26.0	26.3	26.3	22.0	27.0
115	21.0	25.3	24.7	25.7	25.5
116	22.0	27.0	26.0	25.0	24.0
117	16.7	18.3	24.3	22.7	24.5
118	20.0	21.7	23.3	24.7	24.5
119	17.7	22.7	25.0	26.3	27.5
120	21.3	25.0	28.0	28.0	12.5
121	25.3	23.0	26.0	24.3	22.5
122	21.7	24.3	24.7	25.7	24.5
123	21.0	23.0	24.7	24.0	23.5
124	20.0	23.3	21.7	24.0	21.5
125	21.3	24.7	26.0	30.0	20.5
MEAN	20.4	22.2	23.8	24.6	23.9
S.D.	2.45	4.19	2.12	3.09	3.31
N	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive period intervals.
[b]Baseline is GD6.

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 200 GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20
126	23.0	24.3	23.0	24.7	26.0
127	21.0	23.7	23.7	27.0	26.5
128	21.0	21.7	23.3	16.0	23.0
129	20.0	24.0	25.0	24.0	24.5
130	18.7	22.0	21.3	23.3	24.5
131	20.3	22.3	22.0	20.0	25.0
132	19.7	22.3	22.0	24.0	26.0
133	18.3	17.7	20.7	22.7	25.0
134	17.3	20.0	18.0	21.7	19.0
135	19.0	21.7	17.3	26.0	23.5
136	19.7	22.0	20.3	30.3	17.5
137	18.0	20.7	21.7	25.3	22.5
138	24.7	16.3	23.3	30.0	21.0
139	22.0	24.0	24.3	26.0	22.5
140	15.0	25.7	26.7	24.0	31.5
141	23.3	25.7	29.3	31.0	28.0
142	19.3	22.3	23.0	23.0	22.5
143	22.7	24.3	25.3	26.0	25.0
144	18.3	21.0	23.0	23.3	24.5
145	22.0	24.3	26.7	24.7	24.5
146	21.7	24.0	24.7	26.3	25.0
147	21.3	23.3	25.3	24.7	23.5
148	21.0	17.7	20.0	22.3	19.5
149	20.7	23.7	21.7	24.3	29.5
150	18.3	21.0	22.0	24.3	23.5
MEAN	20.3	22.2	22.9	24.6	24.1
S.D.	2.16	2.41	2.70	3.14	3.07
N	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive period intervals.
[b]Baseline is GD6.

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 200 GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20
151	19.3	22.0	23.0	24.3	24.0
152	20.0	26.3	23.7	27.0	25.0
153	18.3	19.7	20.7	24.0	20.5
154	17.0	22.0	22.0	22.0	20.5
155	18.7	22.0	21.0	19.3	21.0
156	14.3	18.3	23.0	23.7	24.0
157	15.0	20.0	20.0	22.7	21.0
158	20.7	21.7	21.0	24.3	22.5
159[c]	--	--	--	--	--
160	16.0	20.3	19.3	22.0	21.0
161	18.7	21.0	19.0	21.7	21.0
162	21.3	19.0	20.7	22.7	21.0
163	18.7	22.0	21.7	23.0	21.0
164	18.3	22.0	23.7	20.7	27.5
165	17.7	19.7	22.7	21.0	23.5
166	19.0	20.7	21.3	20.0	19.5
167	18.0	21.7	22.0	24.3	23.5
168	22.0	25.3	25.7	25.7	26.5
169	18.7	22.3	22.3	20.3	18.5
170	19.7	18.0	26.3	19.7	19.0
171	16.7	20.7	26.3	24.0	29.5
172	17.3	23.3	22.7	24.3	23.5
173	20.3	21.7	23.7	21.0	21.5
174	21.3	21.7	22.7	25.3	26.5
175	21.0	23.7	21.3	23.7	24.0
MEAN	18.7	21.5	22.3	22.8	22.7
S.D.	1.98	1.96	1.95	2.03	2.80
N	24	24	24	24	24

--: Data Unavailable

[a]Calculated daily food consumption for successive period intervals.
[b]Baseline is GD6.
[c]F_0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 200 GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	GD 9[b]	GD 12	GD 15	GD 18	GD 20
176	19.0	14.3	10.7	15.3	17.0
177	18.3	16.3	15.0	17.7	14.0
178	19.3	31.3	16.0	21.0	17.0
179	15.3	12.7	13.7	15.0	16.0
180	20.0	19.3	15.3	15.0	14.0
181	18.0	12.7	16.7	14.7	19.5
182	15.3	7.7	18.0	17.3	18.0
183	19.3	19.0	17.0	22.7	18.0
184	19.7	19.3	17.0	21.0	19.5
185	19.0	18.3	13.7	19.3	18.5
186	17.7	15.7	12.7	16.7	16.0
187	19.7	18.0	15.7	17.0	17.5
188	15.0	17.0	17.3	18.3	20.0
189	12.3	15.3	16.7	15.7	16.5
190	9.0	17.3	17.3	19.0	18.0
191	17.7	19.3	18.3	21.7	22.0
192	13.3	16.3	18.0	18.7	17.0
193	16.7	17.3	21.3	22.0	20.5
194	18.7	15.0	17.3	22.0	20.0
195	20.7	21.7	20.7	18.7	21.5
196	19.3	18.7	16.0	20.3	17.5
197	18.7	18.7	17.3	17.7	16.5
198	17.3	16.0	16.3	21.0	16.5
199	12.7	13.7	15.7	16.3	16.0
200	17.0	18.0	19.3	21.3	17.5
MEAN	17.2	17.2	16.5	18.6	17.8
S.D.	2.87	4.12	2.32	2.52	2.05
N	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive period intervals.
[b]Baseline is GD6.

APPENDIX E

INDIVIDUAL F_0 GENERATION GESTATION DURATION

INDIVIDUAL ANIMAL REPORT BY GROUP

STUDY ID: 200F0
STUDY NO: 200F0

SEX: FEMALE

Animal ID	DUR[a] days
GROUP: 1-F:0 mg base/kg/day	
101	22.00
102	22.00
103	22.00
104	22.00
105	22.00
106	22.00
107	22.00
108	22.00
109	22.00
110	22.00
111	22.00
112	22.00
113	22.00
114	21.00
115	21.00
116	22.00
117	22.00
118	22.00
119	22.00
120	21.00
121	22.00
122	21.00
123	21.00
124	21.00
125	22.00
MEAN	21.76
SD	0.436
N	25

[a]DUR = Gestation Duration.

INDIVIDUAL ANIMAL REPORT BY GROUP

STUDY ID: 200FO
STUDY NO: 200FO

SEX: FEMALE

Animal ID	DUR[a] days
GROUP: 2-F:2 mg base/kg/day	
126	22.00
127	22.00
128	22.00
129	22.00
130	22.00
131	22.00
132	22.00
133	22.00
134	22.00
135	22.00
136	22.00
137	22.00
138	22.00
139	22.00
140	21.00
141	22.00
142	21.00
143	22.00
144	22.00
145	21.00
146	21.00
147	21.00
148	22.00
149	21.00
150	22.00
MEAN	21.76
SD	0.436
N	25

[a]DUR = Gestation Duration.

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP

STUDY ID: 200FO
STUDY NO: 200FO

SEX: FEMALE

Animal ID	DUR[a] days
GROUP: 3-F:6 mg base/kg/day	
151	22.00
152	22.00
153	22.00
154	22.00
155	22.00
156	22.00
157	22.00
158	21.00
159[b]	--
160	22.00
161	22.00
162	22.00
163	22.00
164	21.00
165	21.00
166	21.00
167	21.00
168	21.00
169	21.00
170	22.00
171	21.00
172	21.00
173	22.00
174	22.00
175	21.00
MEAN	21.58
SD	0.504
N	24

[a]DUR = Gestation Duration.
[b]F_0 dam No. 159 was not pregnant.

(--) - Data Unavailable

INDIVIDUAL ANIMAL REPORT BY GROUP

STUDY ID: 200FO
STUDY NO: 200FO

SEX: FEMALE

Animal ID	DUR[a] days
GROUP: 4-F:18 mg base/kg/day	
176	22.00
177	22.00
178	22.00
179	22.00
180	22.00
181	22.00
182	22.00
183	22.00
184	22.00
185	22.00
186	22.00
187	22.00
188	22.00
189	21.00
190	22.00
191	21.00
192	21.00
193	21.00
194	21.00
195	21.00
196	21.00
197	21.00
198	22.00
199	21.00
200	22.00
MEAN	21.64
SD	0.490
N	25

[a]DUR = Gestation Duration.

APPENDIX F

INDIVIDUAL F_0 GENERATION GROSS NECROPSY OBSERVATIONS

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

F_0 Generation: Individual Gross Necropsy Observations

0 mg base/kg/day

Dam No. 123: multiple round, raised areas throughout the jejunum and ileum

2 mg base/kg/day

Dam No. 141: five raised areas on the jejunum
Dam No. 149: multiple round, raised areas throughout the jejunum and ileum
Dam No. 150: five raise areas on the duodenum and jejunum
Dam No. 171: all lobes of the lungs mottled

6 mg base/kg/day

Dam No. 163: raised areas throughout the jejunum and ileum
Dam No. 174: foci on all lobes of the lungs

18 mg base//kg/day

Dam No. 188: multiple round, raised areas throughout the jejunum and ileum
Dam No. 189: right uterus dark in color with two cysts and blood in the uterine horn
Dam No. 192: nodule on the left uterine horn

APPENDIX G

INDIVIDUAL F_1 GENERATION OBSERVATIONS (Clinical Signs)

- Preweaning Period
- Postweaning Period

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Individual Litter Preweaning Clinical Signs Data

Dose Level (mg base/kg/day)	Litter No.	Postnatal Day 0	Postnatal Day 4[a]	Postnatal Day 7	Postnatal Day 14	Postnatal Day 21
0	101M/F[b]	N/HT (2)[c]	N/N	N/Scab (1)[c]	N/N	N/N
	10[illegible]M/F	N/N	N/N	N/N	N/N	N/N
	103M/F	N/N	N/N	Scab (1)/N	N/N	N/N
	104M/F	N/N	N/N	N/N	N/N	N/N
	105M/F	N/N	N/N	N/N	N/N	N/N
	106M/F	N/N	N/N	N/N	N/N	N/N
	107M/F	HT (1)/N	N/N	N/N	N/N	N/N
	10[illegible]M/F	HT (1)/HT (1)	N/N	N/N	N/N	N/N
	109M/F	HT (1)/N	N/N	N/N	N/N	N/N
	110M/F	N/HT (1)	N/N	N/N	N/N	N/N
	111M/F	N/N	N/N	N/N	N/N	N/N
	12[illegible]M/F	N/N	N/N	N/N	N/N	N/N
	11[illegible]M/F	N/N	N/N	N/N	N/N	N/N
	116M/F	N/HT (2)	N/N	N/N	N/N	N/N
	116M/F	N/HT (1)	N/N	N/N	N/N	N/N
	116M/F	N/N	N/N	N/N	N/N	N/N
	11[illegible]M/F	HT (1)/N	N/N	N/N	N/N	N/N
	11[illegible]M/F	N/N	N/N	N/N	N/N	N/N
	11[illegible]M/F	N/N	N/N	N/N	N/N	N/N
	120M/F	N/N	N/N	N/N	N/N	N/N
	116M/F	N/N	M (1)/N	N/N	N/N	N/N
	122M/F	N/N	D (1)/N	N/N	N/N	N/N
	123M/F	N/N	N/N	N/N	N/N	N/N
	124M/F	N/N	N/N	N/N	N/N	N/N
	125M/F	N/N	N/N	N/N	N/N	N/N

[a]Litters culled to 4/sex, when possible, after all data was collected on postnatal day 4
[b]M/F = Male pups/Female pups
[c]The number in parenthesis is the number of pups displaying the clinical sign

N = Normal
HT = Hematoma
M = Missing (presumed dead/cannibalized)
D = Dead

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Individual Litter Preweaning Clincal Signs Data

DRAFT

Dose Level (mg base/kg/day)	Litter No.	Postnatal Day 0	Postnatal Day 4[a]	Postnatal Day 7	Postnatal Day 14	Postnatal Day 21
2	126M/F[b]	HT (1)[c]/N	N/N	N/N	N/N	N/N
	127M/F	HT (1)/HT (1)	N/N	N/N	N/N	N/N
	128M/F	HT (2)/N	N/N	N/N	N/N	N/N
	129M/F	N/N	N/N	N/N	N/N	N/N
	130M/F	N/N	N/N	N/N	N/N	N/N
	131M/F	N/HT (1)	N/N	N/N	N/N	N/N
	132M/F	HT (1)/N	N/N	N/N	N/N	N/N
	133M/F	N/HT (1)	N/N	N/N	N/N	N/N
	134M/F	N/N	N/N	N/N	N/N	N/N
	135M/F	N/HT (1)	N/N	N/N	N/N	N/N
	136M/F	N/N	N/N	N/N	N/N	N/N
	137M/F	N/N	N/N	N/N	N/N	N/N
	138M/F[d]	-/-	N/N	N/N	N/N	N/N
	139M/F	N/IC (1)	N/N	N/N	N/N	N/N
	140M/F	N/N	N/N	N/N	N/N	N/N
	141M/F	N/N	N/N	N/N	N/N	N/N
	142M/F	N/N	N/N	N/N	N/N	N/N
	143M/F	N/N	N/N	N/N	N/N	N/N
	144M/F	N/N	N/N	N/N	N/N	N/N
	145M/F	N/N	N/N	N/N	Abrasion (1)/N	N/N
	146M/F	N/N	N/N	N/N	N/N	N/N
	147M/F	N/N	N/N	N/N	N/N	N/N
	148M/F	N/N	N/N	N/N	N/N	N/N
	149M/F	N/HT,IB,NA (1)	N/M (1)	N/N	N/N	N/N
	150M/F	N/N	N/M (1)	N/N	N/N	N/N

[a]Litters culled to 4/sex, when possible, after all data was collected on postnatal day 4
[b]M/F = Male pups/Female pups
[c]The number in parenthesis is the number of pups displaying the clinical sign
[d]Observations for litter No. 138 inadvertently not recorded on postnatal day 0
N = Normal

HT = Hematoma
M = Missing (presumed dead/cannibalized)
D = Dead
IB = Intermittent breathing
NA = No activity
IC = Indented cranial area

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Individual Litter Preweaning Clincal Signs Data

DRAFT

Dose Level (mg base/kg/day)	Litter No.	Postnatal Day 0	Postnatal Day 4[a]	Postnatal Day 7	Postnatal Day 14	Postnatal Day 21
6	151M/F[b]	N/N	N/N	N/N	N/N	N/N
	168M/F	N/N	N/N	N/N	N/N	N/N
	168M/F	N/N	N/N	N/N	N/N	N/N
	162M/F	N/N	N/N	N/N	N/N	N/N
	168M/F	N//HT (1)[c]	N/N	N/N	N/N	N/N
	167M/F	HT (1)/HT (1)	N/N	N/N	N/N	N/N
	168M/F	N/N	N/N	N/N	N/N	N/N
	168M/F	HT (2)/N	M (1)/N	Scab (1)/N	N/N	N/N
	159[d]	-	-	-	-	-
	167M/F	N/N	N/N	N/N	N/N	N/N
	167M/F	N/N	N/N	N/N	N/N	N/N
	162M/F	N/N	N/N	N/N	N/N	N/N
	168M/F	N/HT (1)	N/N	N/N	N/N	N/N
	164M/F	N/N	N/N	N/N	N/N	N/N
	168M/F	HT (1)/HT (1)	N/N	N/N	N/N	N/N
	166M/F	N/HT (1)	N/N	N/N	N/N	N/N
	167M/F	N/HT (1)	N/N	N/N	N/N	N/N
	168M/F	HT (1)/N	N/N	N/N	N/N	N/N
	169M/F	N/N	N/N	N/N	N/N	N/N
	170M/F	N/HT (1)	N/M(1)	N/N	N/N	N/N
	170M/F	N/N	N/N	N/N	N/N	N/N
	172M/F	N/N	N/N	N/N	N/N	N/N
	173M/F	N/N	M (1)/N	N/N	N/N	N/N
	174M/F	N/N	N/N	N/N	N/N	N/N
	175M/F	N/N	N/N	N/N	N/N	N/N

[a]Litters culled to 4/sex, when possible, after all data was collected on postnatal day 4
[b]M/F = Male pups/Female pups
[c]The number in parenthesis is the number of pups displaying the clinical sign
[d]There was no litter No. 159 since F_0 dam No. 159 was not pregnant

N = Normal
HT = Hematoma
M = Missing (presumed dead/cannibalized)
D = Dead

ORAL PRENATAL AND POSTNATAL DEVELOPMENT STUDY OF WR238605 SUCCINATE IN RATS

F_1 Generation: Individual Litter Preweaning Clincal Signs Data DRAFT

Dose Level (mg base/kg/day)	Litter No.	Postnatal Day 0	Postnatal Day 4[a]	Postnatal Day 7	Postnatal Day 14	Postnatal Day 21
18	176M/F[b]	N/N	N/D (1)[c]	N/N	N/N	N/N
	177M/F	N/N	N/N	Scab (1)/N	N/N	N/N
	178M/F	N/N	N/N	N/N	N/N	N/N
	179M/F	N/N	N/N	N/N	N/N	N/N
	180M/F	HT (1)/N	N/N	N/N	N/N	N/N
	181M/F	N/HT (1)	N/N	N/N	N/N	N/N
	182M/F	N/N	N/N	N/N	N/N	N/N
	183M/F	N/N	N/N	N/N	N/N	N/N
	184M/F	N/N	Scab (1)/N	N/N	N/N	N/N
	185M/F	N/N	N/N	N/N	N/N	N/N
	186M/F	N/N	N/N	N/N	N/N	N/N
	187M/F	N/N	N/N	N/N	N/N	N/N
	188M/F	N/N	N/N	N/N	N/N	N/N
	189M/F	N/N	N/N	N/N	N/N	N/N
	190M/F	HT (1)/N	N/M (1)	N/N	N/N	N/N
	191M/F	N/N	N/N	N/N	N/N	N/N
	192M/F	HT (1)/HT (1)	M (1)/N	N/N	N/N	N/N
	193M/F	HT (1)/N	M (1)/N	N/N	N/N	N/N
	194M/F	N/N	M (1)/N	N/N	N/N	N/N
	195M/F	N/N	N/N	N/N	N/N	N/N
	196M/F	N/N	N/N	N/N	N/N	N/N
	197M/F	N/HT (1)	N/N	N/N	N/N	N/N
	198M/F	N/N	N/N	N/N	N/N	N/N
	199M/F	N/N	N/N	N/N	N/N	N/N
	200M/F	N/N	N/N	N/N	N/N	N/N

[a]Litters culled to 4/sex, when possible, after all data was collected on postnatal day 4
[b]M/F = Male pups/Female pups
[c]The number in parenthesis is the number of pups displaying the clinical sign

N = Normal
HT = Hematoma
M = Missing (presumed dead/cannibalized)
D = Dead

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1011	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1013	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1021	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1024	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1032	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1036	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1043	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1047	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1052	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1054	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1065	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1066	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1071	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1072	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1083	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1084	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1091	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1097	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1102	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1104	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1112	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1113	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1125	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1127	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1135	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1136	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1146	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1148	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1152	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1153	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1161	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1162	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1173	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1174	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1185	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1189	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1192	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1193	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1202	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1203	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1214	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1215	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1223	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1226	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1233	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1236	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1242	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1248	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1251	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
12515	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
10112	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10113	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10214	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10217	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10315	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10318	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10412	Dehydrated			PND 56
	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
10413	Normal			PND 28-PND 70
	Normal			PND 77-PND 91

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
10413 (contd.)	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10511	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10513	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 97
10614	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10616	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10712	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
10713	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
10813	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
10815	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
10911	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
11012	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
11015	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
11111	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
11117	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
11212	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
11213	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
11315	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
11316	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
11412	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11414	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
11511	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11519	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
11611	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11612	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
11711	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11712	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
11812	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11814	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
11911	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
11915	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 96
12012	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12013	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
12113	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
12114	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
12211	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12213	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
PND 28-PND 126 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
12312	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12313	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
12411	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12413	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 97
12511	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
12519	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1264	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1267	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1275	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1277	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1283	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1286	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1295	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1296	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1307	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1309	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1311	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1312	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1322	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1323	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1331	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1333	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1341	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1343	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1353	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1354	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1361	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1365	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1375	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1379	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2(mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1382	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1383	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1392	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1394	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1401	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1404	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1414	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1415	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1421	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1428	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1432	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1434	Dehydrated			PND 63
	Normal			PND 28-PND 56
	Normal			PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1443	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1444	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1452	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1454	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1461	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1463	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1474	Dark Material Around Eyes			PND 42-PND 56
	Dark Material Around Eyes			PND 70
	Normal			PND 28-PND 35
	Normal			PND 63
	Scheduled Sacrifice			PND 71

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1475	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1483	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1484	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1491	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1493	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1501	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1503	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
12611	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12612	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
12715	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12716	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
12813	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12815	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
12911	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
12912	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 98

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
13011	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
13013	Dehydrated			PND 70
	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
13113	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
13114	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
13212	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13213	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
13315	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13317	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
13412	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13414	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
13512	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13515	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
13612	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13614	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
13711	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13713	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
13811	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
13815	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
13912	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
13913	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14011	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14014	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
14111	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14112	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14212	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14213	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
14314	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14315	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14412	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14416	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14511	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14514	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14613	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14615	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
14712	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14714	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
PND 28-PND 126 DOSE: 2 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
14811	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
14812	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
14913	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
14916	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
15011	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
15013	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1511	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1515	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1523	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1524	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1532	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1533	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1542	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1544	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1554	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1555	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1561	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1566	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1571	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1574	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1584	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1585	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

There was no F_1 litter No. 159 since F_0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1603	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1605	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1611	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1612	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1622	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1625	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1634	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1636	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1644	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1646	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1652	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1658	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1661	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1664	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1672	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1673	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1681	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1685	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1691	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1692	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1704	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1706	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1714	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1715	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1723	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1727	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1733	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1734	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1741	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1743	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1754	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1755	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
15112	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15115	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
15211	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15213	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
15313	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15314	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
15412	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15416	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
15513	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15518	Dehydrated			PND 56
	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
15611	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15617	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
15712	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
15714	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
15814	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
15816	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
16011	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
16015	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
16113	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
16114	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
16211	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
16216	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
16311	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16313	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
16412	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16413	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
16513	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16514	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
16613	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16614	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
16711	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16714	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
16813	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16814	Dehydrated			PND 56
	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
16911	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
16913	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
17016	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
17018	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
17111	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17115	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
17212	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17215	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
17311	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
PND 28-PND 126 DOSE: 6 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
17312	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
17411	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
17413	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
17513	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17516	Normal			PND 28-PND 70
	Normal			PND 77
	Normal			PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1762	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1763	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1773	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1774	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1782	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1783	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1792	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1795	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1801	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1806	Dehydrated			PND 56
	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1813	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1814	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
1823	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1824	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1831	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1835	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1845	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1846	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1852	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1853	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1861	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1865	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
1873	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
1875	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1882	Dark Material Around Eyes			PND 56
	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1883	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1894	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1897	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1901	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1904	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1912	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1914	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1921	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1924	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1934	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1936	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
1941	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1942	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1952	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1956	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1962	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1965	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
1972	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1974	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
1982	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
1988	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111
1991	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
1993	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
2005	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
2008	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
17614	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17616	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 97
17712	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17713	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
17815	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17816	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
17911	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
17912	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
18013	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
18014	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
18112	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
18116	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 126
18213	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18214	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
18315	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18317	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
18411	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18416	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
18511	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18515	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
18611	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18613	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125
18712	Normal			PND 28-PND 63
	Scheduled Sacrifice			PND 71
18714	Normal			PND 28-PND 63
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Normal			PND 112
	Normal			PND 119
	Scheduled Sacrifice			PND 125

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
18812	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
18815	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 97
18911	Dark Material Around Eyes			PND 28-PND 70
	Scheduled Sacrifice			PND 71
18912	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98
	Scheduled Sacrifice			PND 105
19012	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19019	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
19112	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19114	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
19214	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19215	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
19315	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19317	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 113
19415	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19416	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
19512	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19514	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
19613	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19617	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
19715	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19716	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112

DRAFT

INDIVIDUAL CLINICAL SIGNS (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
PND 28-PND 126 DOSE: 18 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
19812	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Scheduled Sacrifice			PND 97
19814	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
19912	Normal			PND 28-PND 70
	Scheduled Sacrifice			PND 71
19915	Normal			PND 28-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 112
20011	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Scheduled Sacrifice			PND 71
20012	Normal			PND 28-PND 49
	Normal			PND 63-PND 70
	Normal			PND 77-PND 91
	Normal			PND 98-PND 105
	Scheduled Sacrifice			PND 111

APPENDIX H

INDIVIDUAL F_1 GENERATION BODY WEIGHTS AND WEIGHT GAIN

- Preweaning Period
- Postweaning Period

PREWEANING PERIOD: INDIVIDUAL LITTER BODY WEIGHTS AND BODY WEIGHT GAIN

Note: During the preweaning period, the litter was the experimental unit. Thus, the pup body weights and weight gain group means were derived in two steps. First, the individual pup body weights were used to determine the mean for each litter. Second, the litter means were used to determine the mean for each group. The individual pup body weights are located on pages H19 through H65.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
101	7.0	11.7	18.6	36.2	58.5
102	6.7	11.0	16.9	34.5	56.8
103	7.4	12.1	19.6	40.3	62.7
104	7.1	12.1	18.5	38.4	60.5
105	6.9	11.6	18.7	38.2	60.0
106	6.3	11.1	17.6	36.7	57.9
107	6.9	12.5	18.3	36.3	56.2
108	7.4	12.3	18.6	36.1	58.6
109	6.9	11.9	19.0	36.0	54.4
110	6.7	10.7	17.1	35.6	55.3
111	7.7	12.4	19.0	36.6	59.5
112	6.7	10.7	16.2	33.7	52.7
113	6.6	10.9	18.1	36.4	59.0
114	6.1	9.3	14.9	32.7	50.7
115	6.0	9.7	15.5	31.1	48.2
116	6.9	11.9	18.4	35.6	56.5
117	6.5	10.7	17.3	37.8	59.2
118	6.5	11.0	17.0	38.4	59.9
119	7.4	11.9	18.7	37.2	57.6
120	6.2	9.6	14.8	31.0	48.9
121	6.6	10.2	16.8	33.9	53.0
122	6.1	9.7	14.6	31.8	48.3
123	6.1	9.7	15.9	33.9	50.2
124	5.7	8.2	14.4	32.2	48.7
125	6.5	11.0	19.0	38.4	55.1
MEAN	6.7	11.0	17.3	35.6	55.5
S.D.	0.50	1.13	1.58	2.50	4.34
N	25	25	25	25	25

--: Data Unavailable

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
126	7.1	12.0	19.8	40.1	63.1
127	7.5	10.8	16.9	34.5	54.9
128	6.5	10.8	16.6	33.7	54.9
129	7.0	12.5	20.8	43.0	64.7
130	7.1	12.2	19.5	38.3	61.7
131	6.9	10.8	17.7	39.1	58.9
132	7.0	12.2	20.1	41.9	66.3
133	6.8	11.0	17.5	34.7	56.0
134	7.3	11.0	16.4	32.0	52.4
135	7.0	12.4	18.6	35.3	59.1
136	7.1	11.5	17.2	31.8	49.6
137	6.7	10.7	17.3	34.3	50.0
138[a]	--	11.1	18.0	33.8	54.9
139	6.5	11.0	17.5	34.7	55.0
140	6.3	10.1	15.3	31.9	50.1
141	7.3	11.9	19.0	39.3	57.6
142	5.7	9.0	15.7	34.4	51.5
143	6.6	10.5	16.3	33.7	54.8
144	7.0	9.4	14.6	30.2	49.3
145	6.0	9.9	14.8	29.3	39.4
146	6.1	9.7	15.8	35.4	54.3
147	5.7	8.9	14.3	30.8	47.3
148	6.4	10.6	16.7	33.0	53.8
149	6.3	11.5	17.2	35.8	54.2
150	6.8	11.0	16.9	33.1	51.5
MEAN	6.7	10.9	17.2	35.0	54.6
S.D.	0.49	1.01	1.72	3.54	5.83
N	24	25	25	25	25

--: Data Unavailable

[a]The PND0 body weights for this litter were inadvertently not recorded.

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
151	7.1	12.1	19.3	38.8	62.6
152	6.5	10.5	16.6	35.5	56.6
153	7.0	11.1	16.6	33.7	53.4
154	6.4	10.5	17.0	34.7	55.5
155	6.5	10.2	16.7	36.3	59.5
156	6.5	10.0	16.2	34.5	55.5
157	6.8	10.8	17.4	35.3	56.9
158	5.5	9.5	15.2	31.0	49.6
159[a]	--	--	--	--	--
160	6.5	9.9	16.5	33.2	52.4
161	6.2	10.2	15.6	30.6	47.9
162	6.8	11.8	18.4	36.3	54.5
163	6.4	10.0	16.1	32.9	52.0
164	6.0	9.6	14.6	32.5	48.3
165	6.1	9.6	15.0	33.6	54.8
166	5.6	9.2	14.9	31.7	50.0
167	5.7	9.8	15.4	33.1	49.8
168	6.4	9.6	15.8	33.7	52.7
169	6.0	10.2	15.3	31.9	49.0
170	6.1	9.1	15.1	33.9	55.8
171	6.5	10.3	16.0	32.8	53.0
172	5.8	8.1	13.0	30.2	46.7
173	7.8	12.9	21.1	40.8	61.6
174	7.1	11.8	18.9	39.3	62.5
175	6.7	9.2	14.1	29.5	46.0
MEAN	6.4	10.2	16.3	34.0	53.6
S.D.	0.53	1.08	1.78	2.82	4.80
N	24	24	24	24	24

--: Data Unavailable

[a]There was no F_1 litter since F_0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
176	6.3	11.1	17.1	32.8	51.5
177	6.2	9.7	14.9	28.0	48.0
178	6.6	10.1	15.5	27.7	46.5
179	6.5	10.1	15.8	32.4	53.0
180	6.0	9.1	13.8	26.2	43.8
181	6.7	10.3	15.4	30.0	49.9
182	6.3	9.6	14.1	28.8	47.9
183	6.6	10.3	17.4	35.0	56.4
184	6.1	9.6	13.7	27.6	46.1
185	6.9	10.8	16.1	29.7	50.7
186	6.0	9.3	14.0	27.5	42.0
187	6.7	10.6	15.8	29.1	47.5
188	6.6	10.1	16.4	31.8	51.3
189	5.2	7.6	12.2	25.7	40.3
190	5.9	7.5	11.7	25.4	42.4
191	6.0	9.9	15.0	30.1	47.2
192	5.6	8.5	11.9	24.6	40.3
193	5.6	8.1	13.0	28.4	43.2
194	6.2	9.1	14.5	31.5	51.9
195	6.2	9.0	14.2	29.0	45.5
196	5.8	9.0	13.6	25.1	43.1
197	6.3	8.3	12.5	25.4	40.6
198	6.8	10.0	15.7	28.7	47.3
199	5.3	7.2	10.9	24.2	38.5
200	6.5	9.9	15.2	30.6	50.9
MEAN	6.2	9.4	14.4	28.6	46.6
S.D.	0.46	1.04	1.70	2.80	4.64
N	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PNO 0	PNO 4	PNO 7	PND 14	PND 21
101F	6.6	11.1	17.6	34.2	55.8
102F	6.2	10.6	16.2	33.7	55.2
103F	6.3	10.8	17.9	37.3	57.6
104F	6.6	11.4	17.7	36.9	55.7
105F	6.6	10.3	17.0	35.2	53.0
106F	5.7	10.5	16.9	35.6	55.5
107F	6.5	12.0	17.6	35.5	54.1
108F	6.8	11.3	17.3	33.8	56.0
109F	6.6	11.2	17.8	34.7	52.7
110F	6.6	10.5	17.0	35.0	53.7
111F	6.9	11.5	17.2	33.1	51.6
112F	6.3	9.8	15.8	33.2	52.3
113F	6.0	10.2	16.8	33.8	54.9
114F	5.8	9.0	15.0	33.4	52.9
115F	5.6	8.7	14.1	29.5	45.0
116F	6.6	11.3	17.7	34.8	54.4
117F	6.0	9.5	16.0	35.6	54.3
118F	6.0	10.7	16.4	37.1	57.2
119F	6.9	11.0	17.7	36.1	54.8
120F	5.8	8.9	14.3	29.6	47.5
121F	6.2	9.6	15.4	32.5	50.1
122F	5.9	9.1	13.6	30.4	47.3
123F	5.9	9.5	15.6	32.6	48.6
124F	5.3	7.5	12.9	30.0	43.9
125F	6.2	10.1	17.0	36.3	55.2
MEAN	6.2	10.2	16.3	34.0	52.8
S.D.	0.43	1.07	1.43	2.27	3.71
N	25	25	25	25	25

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
126F	7.1	11.5	18.3	37.9	58.4
127F	6.8	9.9	15.3	32.0	49.6
128F	6.5	10.9	16.8	33.1	53.6
129F	6.8	11.5	19.1	39.9	58.6
130F	6.9	11.6	18.9	37.9	60.3
131F	6.5	10.6	17.0	37.3	55.9
132F	6.8	12.1	20.0	41.2	64.2
133F	6.3	10.6	16.4	33.9	53.2
134F	6.8	10.6	15.4	30.1	51.4
135F	6.7	11.9	17.7	34.4	55.2
136F	7.2	11.9	18.0	33.5	52.5
137F	6.3	10.4	16.5	33.0	50.3
138F[a]	--	10.1	16.4	32.1	52.8
139F	6.3	10.6	16.6	33.3	52.0
140F	6.0	9.4	14.2	30.3	46.5
141F	6.2	10.0	16.0	34.6	51.2
142F	5.6	8.9	15.1	33.4	49.3
143F	6.3	9.8	15.1	31.2	49.5
144F	6.4	8.8	13.5	28.2	46.8
145F	5.7	8.9	13.6	27.2	37.0
146F	6.0	9.3	14.7	33.6	50.3
147F	5.1	8.3	13.5	29.6	44.7
148F	6.1	10.1	16.3	32.4	51.8
149F	6.1	11.0	15.6	32.3	49.6
150F	6.5	10.8	15.9	31.1	48.5
MEAN	6.4	10.4	16.2	33.3	51.7
S.D.	0.49	1.06	1.74	3.41	5.45
N	24	25	25	25	25

--: Data Unavailable

[a]The PND0 body weights for this litter were inadvertently not recorded.

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
151F	6.8	11.5	18.1	36.8	59.5
152F	5.9	9.5	15.3	33.7	53.2
153F	6.8	10.8	16.7	33.5	53.3
154F	6.0	10.1	16.0	32.8	52.0
155F	6.4	10.0	16.4	34.1	54.7
156F	6.2	9.8	16.1	34.1	54.2
157F	6.4	10.1	16.4	34.5	54.5
158F	5.6	9.2	14.9	30.9	48.8
159F[a]	--	--	--	--	--
160F	6.1	10.0	15.5	32.4	51.7
161F	5.9	9.6	14.6	28.6	45.9
162F	6.4	11.1	17.4	35.1	52.0
163F	6.0	9.4	14.6	30.0	47.4
164F	5.8	8.8	13.4	30.4	46.4
165F	5.8	9.1	14.3	31.5	51.3
166F	5.3	8.8	14.2	30.2	48.5
167F	5.4	9.1	13.9	30.7	45.8
168F	5.9	9.1	15.2	32.9	50.6
169F	5.6	9.8	14.8	30.4	47.2
170F	5.7	8.5	14.3	33.5	53.3
171F	6.1	9.8	15.4	31.1	49.4
172F	5.5	7.7	12.2	29.3	45.2
173F	7.2	10.6	18.3	37.0	56.8
174F	6.5	10.8	17.7	37.2	58.8
175F	6.2	8.6	13.6	28.9	44.6
MEAN	6.1	9.7	15.4	32.5	51.0
S.D.	0.46	0.90	1.55	2.53	4.24
N	24	24	24	24	24

--: Data Unavailable

[a]There was no F_1 litter since F_0 dam No. 159 was not pregnant.

INDIVIDUAL BODY WEIGHTS (Grams) (Preweaning Period)

STUDY: 200P GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 0	PND 4	PND 7	PND 14	PND 21
176F	6.0	10.9	16.9	32.0	49.9
177F	5.8	9.1	13.6	26.5	46.5
178F	6.6	9.5	14.2	25.6	44.0
179F	6.1	10.0	15.5	32.0	52.2
180F	5.7	8.7	13.7	26.2	45.5
181F	6.1	9.3	13.6	26.0	41.3
182F	6.0	9.2	12.9	26.1	44.1
183F	6.0	9.4	15.8	32.8	52.7
184F	5.9	9.4	13.9	27.4	44.7
185F	6.3	9.9	14.4	27.2	45.9
186F	5.7	8.8	14.0	26.7	40.8
187F	6.4	10.1	15.5	29.4	48.0
188F	6.0	9.0	14.2	29.5	46.6
189F	4.8	6.5	9.9	21.9	31.9
190F	5.8	7.5	11.4	24.2	40.5
191F	5.9	9.6	15.3	30.1	49.2
192F	5.3	7.9	11.2	23.0	38.4
193F	5.3	7.8	12.3	27.6	41.4
194F	6.1	9.0	14.4	30.8	50.6
195F	5.7	8.3	13.6	28.6	43.5
196F	5.6	8.4	13.1	24.2	40.7
197F	5.6	7.7	11.9	23.9	38.8
198F	6.6	9.8	15.5	27.4	45.3
199F	5.1	7.1	11.0	23.8	37.4
200F	6.2	9.7	15.2	30.7	51.4
MEAN	5.9	8.9	13.7	27.3	44.4
S.D.	0.43	1.04	1.71	3.01	5.12
N	25	25	25	25	25

--: Data Unavailable

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
101	4.7	6.8	17.7	22.3	51.5
102	4.3	6.0	17.6	22.3	50.1
103	4.7	7.5	20.7	22.4	55.3
104	5.0	6.4	19.9	22.2	53.5
105	4.7	7.1	19.5	21.8	53.1
106	4.8	6.5	19.1	21.3	51.6
107	5.6	5.8	18.1	19.8	49.2
108	4.9	6.3	17.5	22.5	51.2
109	5.0	7.1	17.0	18.4	47.5
110	4.0	6.4	18.5	19.8	48.6
111	4.7	6.6	17.6	22.9	51.9
112	4.0	5.4	17.5	19.0	46.0
113	4.4	7.2	18.3	22.6	52.5
114	3.2	5.6	17.8	17.9	44.6
115	3.7	5.8	15.6	17.1	42.2
116	5.1	6.5	17.2	20.9	49.7
117	4.2	6.6	20.5	21.4	52.6
118	4.5	5.9	21.4	21.6	53.4
119	4.5	6.8	18.6	20.4	50.2
120	3.4	5.2	16.2	17.9	42.7
121	3.7	6.5	17.1	19.1	46.4
122	3.6	4.9	17.2	16.5	42.3
123	3.7	6.2	17.9	16.4	44.2
124	2.5	6.3	17.8	16.5	43.0
125	4.5	8.1	19.4	16.6	48.5
MEAN	4.3	6.4	18.2	20.0	48.9
S.D.	0.70	0.73	1.39	2.27	3.97
N	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
126	4.9	7.7	20.4	22.9	55.9
127	3.4	6.1	17.7	20.4	47.5
128	4.3	5.8	17.1	21.3	48.4
129	5.5	8.3	22.2	21.7	57.8
130	5.1	7.3	18.8	23.3	54.6
131	3.9	6.9	21.4	19.9	52.0
132	5.2	7.9	21.8	24.5	59.4
133	4.2	6.4	17.3	21.2	49.1
134	3.6	5.4	15.6	20.4	45.1
135	5.4	6.3	16.7	23.8	52.1
136	4.5	5.7	14.6	17.8	42.5
137	4.0	6.6	17.0	15.8	43.4
138[c]	--	6.9	15.8	21.1	43.8
139	4.4	6.6	17.2	20.3	48.5
140	3.8	5.2	16.5	18.2	43.8
141	4.7	7.1	20.3	18.2	50.3
142	3.3	6.7	18.7	17.1	45.8
143	3.9	5.8	17.4	21.1	48.2
144	2.5	5.2	15.6	19.1	42.3
145	3.8	4.9	14.5	10.1	33.4
146	3.6	6.1	19.6	18.9	48.2
147	3.2	5.5	16.5	16.5	41.6
148	4.2	6.1	16.3	20.7	47.3
149	5.2	5.7	18.6	18.4	47.9
150	4.3	5.9	16.2	18.4	44.7
MEAN	4.2	6.3	17.8	19.6	47.7
S.D.	0.76	0.88	2.17	2.99	5.65
N	24	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]The PND0 body weights for this litter were inadvertently not recorded.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
151	5.0	7.3	19.4	23.8	55.5
152	4.0	6.2	18.8	21.1	50.1
153	4.1	5.5	17.1	19.8	46.4
154	4.1	6.5	17.8	20.8	49.0
155	3.7	6.6	19.6	23.2	53.0
156	3.5	6.2	18.3	21.0	49.0
157	3.9	6.6	17.9	21.6	50.1
158	4.0	5.7	15.9	18.6	44.1
159[c]	--	--	--	--	--
160	3.5	6.6	16.7	19.3	46.0
161	4.0	5.4	15.0	17.4	41.8
162	5.0	6.6	17.9	18.3	47.7
163	3.6	6.1	16.8	19.1	45.6
164	3.6	4.9	17.9	15.9	42.3
165	3.5	5.5	18.5	21.2	48.7
166	3.6	5.7	16.8	18.3	44.3
167	4.1	5.6	17.7	16.7	44.1
168	3.2	6.2	17.9	19.0	46.4
169	4.3	5.1	16.6	17.1	43.1
170	3.1	5.9	18.9	21.9	49.8
171	3.8	5.7	16.8	20.2	46.5
172	2.3	5.0	17.2	16.4	40.9
173	5.1	8.2	19.6	20.8	53.8
174	4.7	7.1	20.4	23.3	55.5
175	2.5	5.0	15.4	16.5	39.3
MEAN	3.8	6.1	17.7	19.6	47.2
S.D.	0.70	0.80	1.36	2.30	4.44
N	24	24	24	24	24

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]There was no F_1 litter since F_0 dam No. 159 was not pregnant.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
176	4.8	6.0	15.7	18.8	45.2
177	3.5	5.2	13.1	20.1	41.8
178	3.4	5.5	12.2	18.8	39.9
179	3.7	5.7	16.6	20.6	46.6
180	3.1	4.7	12.4	17.6	37.9
181	3.6	5.1	14.6	19.9	43.2
182	3.3	4.5	14.8	19.1	41.6
183	3.8	7.0	17.7	21.4	49.8
184	3.5	4.0	13.9	18.6	40.0
185	3.9	5.3	13.6	21.1	43.9
186	3.2	4.7	13.5	14.6	36.0
187	3.9	5.2	13.3	18.4	40.9
188	3.4	6.4	15.4	19.6	44.7
189	2.4	4.6	13.5	14.7	35.2
190	1.7	4.2	13.7	17.0	36.6
191	3.8	5.1	15.1	17.2	41.2
192	3.0	3.4	12.6	15.7	34.7
193	2.5	4.9	15.4	14.8	37.6
194	2.9	5.4	17.1	20.4	45.7
195	2.8	5.2	14.8	16.5	39.3
196	3.2	4.5	11.5	18.0	37.3
197	2.1	4.2	12.9	15.2	34.3
198	3.2	5.7	13.0	18.6	40.5
199	2.0	3.7	13.2	14.4	33.3
200	3.4	5.3	15.4	20.3	44.5
MEAN	3.2	5.0	14.2	18.1	40.5
S.D.	0.69	0.82	1.58	2.20	4.31
N	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
101F	4.5	6.5	16.7	21.6	49.2
102F	4.4	5.6	17.4	21.6	49.0
103F	4.5	7.1	19.3	20.4	51.3
104F	4.8	6.3	19.2	18.8	49.1
105F	3.7	6.7	18.3	17.7	46.4
106F	4.8	6.4	18.7	19.9	49.7
107F	5.6	5.6	17.9	18.7	47.7
108F	4.5	6.0	16.5	22.2	49.2
109F	4.6	6.6	17.0	18.0	46.1
110F	3.9	6.6	18.0	18.7	47.1
111F	4.6	5.8	15.9	18.5	44.7
112F	3.5	6.0	17.4	19.1	46.0
113F	4.3	6.6	17.0	21.1	48.9
114F	3.2	6.0	18.3	19.5	47.1
115F	3.1	5.4	15.4	15.5	39.4
116F	4.7	6.4	17.1	19.6	47.7
117F	3.5	6.6	19.5	18.8	48.3
118F	4.7	5.7	20.7	20.1	51.2
119F	4.0	6.7	18.4	18.7	47.9
120F	3.1	5.4	15.3	17.9	41.7
121F	3.5	5.8	17.1	17.6	43.9
122F	3.1	4.5	16.8	16.8	41.4
123F	3.6	6.1	17.1	16.0	42.7
124F	2.2	5.4	17.1	14.0	38.7
125F	3.9	6.9	19.4	18.8	49.0
MEAN	4.0	6.1	17.7	18.8	46.5
S.D.	0.76	0.60	1.33	1.93	3.48
N	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
126F	4.4	6.7	19.7	20.5	51.3
127F	3.1	5.4	16.7	17.6	42.8
128F	4.4	5.9	16.4	20.5	47.1
129F	4.7	7.7	20.7	18.8	51.9
130F	4.8	7.3	19.0	22.4	53.4
131F	4.0	6.4	20.3	18.6	49.4
132F	5.3	7.8	21.2	23.0	57.4
133F	4.3	5.8	17.6	19.3	46.9
134F	3.7	4.9	14.6	21.3	44.5
135F	5.2	5.8	16.7	20.7	48.5
136F	4.7	6.1	15.5	19.1	45.3
137F	4.1	6.1	16.6	17.3	44.0
138F[c]	--	6.3	15.7	20.7	42.8
139F	4.3	6.0	16.7	18.7	45.7
140F	3.4	4.9	16.1	16.2	40.6
141F	3.9	6.0	18.6	16.6	45.0
142F	3.3	6.2	18.3	15.9	43.7
143F	3.5	5.3	16.1	18.3	43.2
144F	2.3	4.7	14.7	18.6	40.4
145F	3.2	4.7	13.6	9.8	31.3
146F	3.2	5.5	18.9	16.7	44.3
147F	3.2	5.2	16.1	15.0	39.5
148F	4.0	6.3	16.1	19.4	45.7
149F	4.9	4.6	16.8	17.2	43.4
150F	4.3	5.1	15.2	17.4	42.0
MEAN	4.0	5.9	17.1	18.4	45.2
S.D.	0.75	0.88	1.99	2.70	5.15
N	24	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]The PND0 body weights for this litter were inadvertently not recorded.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
151F	4.8	6.6	18.7	22.8	52.8
152F	3.5	5.8	18.5	19.5	47.3
153F	4.0	5.9	16.8	19.8	46.5
154F	4.1	5.9	16.7	19.2	45.9
155F	3.7	6.3	17.7	20.6	48.3
156F	3.6	6.3	18.0	20.1	48.0
157F	3.7	6.3	18.1	20.1	48.1
158F	3.6	5.7	16.0	17.8	43.2
159F[c]	--	--	--	--	--
160F	3.9	5.5	16.9	19.4	45.6
161F	3.6	5.0	14.1	17.3	40.0
162F	4.6	6.4	17.7	16.9	45.6
163F	3.4	5.2	15.4	17.4	41.3
164F	3.0	4.7	17.0	15.9	40.6
165F	3.3	5.2	17.2	19.8	45.4
166F	3.5	5.4	16.0	18.3	43.2
167F	3.7	4.8	16.8	15.1	40.4
168F	3.2	6.1	17.7	17.7	44.7
169F	4.2	5.0	15.6	16.8	41.6
170F	2.9	5.8	19.1	19.8	47.6
171F	3.7	5.7	15.7	18.3	43.4
172F	2.1	4.5	17.1	16.0	39.7
173F	3.4	7.7	18.7	19.8	49.6
174F	4.2	7.0	19.4	21.7	52.3
175F	2.4	4.9	15.3	15.7	38.4
MEAN	3.6	5.7	17.1	18.6	45.0
S.D.	0.61	0.77	1.34	1.97	3.92
N	24	24	24	24	24

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.
[c]There was no F_1 litter since F_0 dam No. 159 was not pregnant.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Preweaning Period)

STUDY: 200P GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 4[b]	PND 7	PND 14	PND 21	TOTAL GAIN
176F	4.8	6.0	15.2	17.9	43.9
177F	3.4	4.5	12.9	20.0	40.8
178F	2.9	4.7	11.4	18.4	37.4
179F	3.9	5.5	16.6	20.2	46.1
180F	3.1	4.9	12.5	19.3	39.8
181F	3.2	4.4	12.4	15.3	35.2
182F	3.2	3.7	13.2	18.0	38.2
183F	3.5	6.4	17.1	19.8	46.7
184F	3.5	4.4	13.5	17.3	38.8
185F	3.6	4.5	12.9	18.7	39.6
186F	3.1	5.2	12.8	14.1	35.1
187F	3.7	5.4	13.9	18.6	41.6
188F	3.0	5.2	15.3	17.1	40.6
189F	1.6	3.5	12.0	10.0	27.1
190F	1.7	3.9	12.8	16.3	34.7
191F	3.7	5.8	14.7	19.1	43.2
192F	2.6	3.3	11.8	15.4	33.1
193F	2.5	4.5	15.2	13.9	36.1
194F	2.9	5.5	16.4	19.8	44.5
195F	2.7	5.3	15.0	14.9	37.8
196F	2.8	4.7	11.1	16.5	35.1
197F	2.0	4.2	12.1	14.8	33.1
198F	3.2	5.7	11.9	17.9	38.8
199F	2.0	3.9	12.8	13.7	32.3
200F	3.4	5.6	15.5	20.7	45.2
MEAN	3.0	4.8	13.6	17.1	38.6
S.D.	0.72	0.82	1.73	2.59	4.84
N	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period.
[b]Baseline is PND0.

PREWEANING PERIOD: INDIVIDUAL PUP BODY WEIGHTS

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
10101	7.33	12.31	19.22	37.56	59.94
10102	6.95	11.20	17.64	33.90	56.69
10103	6.96	11.95	18.78	37.19	58.82
10104	6.87	11.49	c	c	c
Mean	7.03	11.74	18.55	36.22	58.48
S.D.	3.00	3.00	3.00	3.00	3.00
10201	7.17	11.61	18.12	36.37	58.66
10202	7.04	11.68	a	a	a
10203	6.30	10.75	16.71	33.79	55.24
10204	5.76	10.36	15.77	33.53	54.62
10205	6.14	9.91	15.99	33.46	56.48
Mean	6.48	10.86	16.65	34.29	56.25
S.D.	0.60	0.77	1.06	1.40	1.78
10301	7.19	11.81	19.26	40.93	61.16
10302	7.23	11.71	18.93	37.33	62.12
10303	7.43	12.20	a	a	a
10304	7.45	12.61	20.62	41.52	62.97
10305	7.51	12.20	a	a	a
10306	7.36	12.08	19.43	41.27	64.46
Mean	7.36	12.10	19.56	40.26	62.68
S.D.	0.13	0.32	0.74	1.97	1.40
10401	7.54	13.00	a	a	a
10402	6.90	12.27	a	a	a
10403	6.70	11.72	18.04	38.54	61.02
10404	6.99	11.66	a	a	a
10405	7.34	12.65	19.37	39.55	61.85
10406	6.96	12.13	18.48	37.88	59.23
10407	7.12	11.42	18.05	37.57	60.05
Mean	7.08	12.12	18.49	38.39	60.54
S.D.	0.28	0.57	0.62	0.88	1.14
10501	7.13	11.84	a	a	a
10502	6.81	11.85	19.38	39.79	63.13
10503	6.82	11.61	18.63	37.64	60.31
10504	6.94	11.28	18.32	37.77	57.81
10505	7.19	11.97	a	a	a
10506	6.72	11.31	18.39	37.52	58.66
10507	6.65	11.21	a	a	a
Mean	6.89	11.58	18.68	38.18	59.98
S.D.	0.20	0.31	0.49	1.08	2.34

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
10601	6.72	11.64	a	a	a
10602	6.59	11.28	a	a	a
10603	6.37	10.62	17.24	35.92	58.19
10604	6.31	11.26	18.36	37.32	59.50
10605	6.02	10.71	17.01	36.57	56.34
10606	6.02	11.00	17.64	36.77	57.70
Mean	6.34	11.09	17.56	36.65	57.93
S.D.	0.29	0.38	0.59	0.58	1.31
10701	6.78	12.33	17.87	35.61	53.40
10702	7.17	12.73	18.64	37.38	57.21
10703	6.84	12.48	18.37	36.04	57.84
Mean	6.93	12.51	18.29	36.34	56.15
S.D.	0.21	0.20	0.39	0.92	2.40
10801	7.51	12.98	19.46	36.44	58.33
10802	7.16	11.46	17.80	35.71	57.58
10803	7.60	12.35	18.68	36.36	59.24
10804	7.44	12.39	18.41	35.93	59.17
Mean	7.43	12.30	18.59	36.11	58.58
S.D.	0.19	0.63	0.69	0.35	0.78
10901	7.33	12.61	20.08	34.73	51.41
10902	6.90	11.86	18.76	37.49	54.67
10903	6.32	11.01	a	a	a
10904	6.82	12.13	a	a	a
10905	7.11	12.58	19.92	38.02	59.87
10906	7.11	12.22	a	a	a
10907	6.41	10.85	17.21	33.89	51.62
Mean	6.86	11.89	18.99	36.03	54.39
S.D.	0.37	0.71	1.33	2.03	3.94
11001	6.33	8.90	15.13	32.95	50.21
11002	6.94	11.42	17.86	36.15	54.59
11003	6.90	11.55	a	a	a
11004	7.18	11.55	18.17	37.49	60.75
11005	6.46	10.52	17.19	35.65	55.76
11006	6.38	10.28	a	a	a
Mean	6.70	10.70	17.09	35.56	55.33
S.D.	0.35	1.04	1.37	1.91	4.33

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
11101	7.76	12.60	19.31	36.09	57.79
11102	7.67	12.24	18.49	34.47	55.64
11103	7.57	12.38	19.15	39.29	65.20
Mean	7.67	12.41	18.98	36.62	59.54
S.D.	0.10	0.18	0.43	2.45	5.02
11201	6.90	10.83	a	a	a
11202	6.74	11.03	a	a	a
11203	6.39	10.50	17.49	35.57	56.57
11204	6.73	10.87	a	a	a
11205	6.48	10.68	17.20	34.31	53.13
11206	6.82	10.97	a	a	a
11207	6.45	10.00	15.05	33.45	51.13
11208	6.58	10.07	14.84	31.35	49.93
11209	7.06	11.53	a	a	a
Mean	6.68	10.72	16.15	33.67	52.69
S.D.	0.23	0.48	1.39	1.77	2.90
11301	6.55	11.00	18.42	37.36	62.84
11302	6.62	11.07	a	a	a
11303	6.51	11.06	a	a	a
11304	7.04	11.88	19.08	37.04	60.27
11305	6.54	10.33	17.65	36.09	57.33
11306	6.07	10.34	17.20	35.20	55.73
11313	6.59	10.69	a	a	a
Mean	6.56	10.91	18.09	36.42	59.04
S.D.	0.28	0.53	0.83	0.98	3.15
11401	6.06	9.21	a	a	a
11402	6.51	9.30	15.85	34.49	56.21
11403	6.08	9.43	a	a	a
11404	6.06	9.39	a	a	a
11405	6.27	9.68	a	a	a
11406	5.95	9.22	14.10	30.62	44.52
11407	6.11	9.11	a	a	a
11408	5.84	9.38	15.18	33.10	50.90
11409	5.95	8.86	14.50	32.76	51.06
Mean	6.09	9.29	14.91	32.74	50.67
S.D.	0.20	0.23	0.77	1.60	4.79

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
11501	6.17	9.90	15.83	32.24	50.88
11502	5.76	9.08	14.75	30.64	46.47
11503	5.77	9.41	15.21	30.70	47.89
11505	6.35	10.24	16.10	30.72	47.54
Mean	6.01	9.66	15.47	31.08	48.20
S.D.	0.30	0.51	0.61	0.78	1.89
11601	6.72	11.43	17.40	34.56	54.40
11602	6.80	11.86	18.56	35.34	56.53
11603	7.02	12.55	19.04	36.79	60.06
11604	6.86	11.82	18.58	35.76	55.14
11617	6.70	11.91	a	a	a
Mean	6.82	11.91	18.40	35.61	56.53
S.D.	0.13	0.40	0.70	0.93	2.51
11701	6.79	11.29	18.76	38.87	61.64
11702	6.29	11.18	a	a	a
11703	6.81	10.81	17.34	37.52	57.39
11704	5.88	9.69	16.09	37.31	59.01
11705	6.24	10.33	17.16	37.55	58.58
11706	6.75	10.57	a	a	a
11707	6.53	10.95	a	a	a
11708	6.97	10.81	a	a	a
11713	4.80	8.05	a	a	a
11714	6.79	10.83	a	a	a
Mean	6.39	10.45	17.34	37.81	59.16
S.D.	0.65	0.96	1.10	0.71	1.79
11801	6.78	10.27	a	a	a
11802	6.24	10.91	16.19	37.04	57.80
11803	6.30	10.93	a	a	a
11804	6.28	10.89	a	a	a
11805	6.89	11.54	17.80	39.59	59.89
11806	6.62	11.50	a	a	a
11807	6.24	11.36	a	a	a
11808	6.50	11.49	17.43	38.98	61.01
11809	6.68	10.49	16.43	37.85	61.05
Mean	6.50	11.04	16.96	38.37	59.94
S.D.	0.25	0.46	0.77	1.14	1.52

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
11901	7.37	11.46	18.49	38.80	58.86
11902	7.17	11.95	19.04	37.41	60.46
11903	7.84	11.98	19.22	38.19	57.94
11904	7.40	12.12	a	a	a
11905	7.16	11.73	17.88	34.52	53.15
Mean	7.39	11.85	18.66	37.23	57.60
S.D.	0.28	0.26	0.60	1.89	3.15
12001	6.26	9.62	a	a	a
12002	6.24	9.80	15.35	31.57	49.70
12003	6.05	9.37	14.23	30.52	45.83
12004	6.22	9.66	14.96	30.22	50.81
12005	5.96	9.39	14.45	31.49	49.17
Mean	6.15	9.57	14.75	30.95	48.88
S.D.	0.13	0.18	0.50	0.68	2.14
12101	6.96	b	b	b	b
12102	6.51	10.66	17.45	34.19	53.92
12103	6.52	10.94	a	a	a
12104	6.51	9.60	16.20	32.35	51.76
12105	6.17	9.78	16.90	33.80	53.51
12106	6.66	10.15	16.48	35.08	52.69
Mean	6.56	10.23	16.76	33.86	52.97
S.D.	0.26	0.57	0.54	1.14	0.96
12201	5.85	8.93	a	a	a
12202	6.15	9.48	14.60	31.74	48.63
12203	5.99	10.02	14.16	31.63	48.67
12204	5.87	b	b	b	b
12205	5.98	9.95	14.71	31.43	48.09
12206	6.45	10.14	14.92	32.43	47.95
12207	6.24	9.13	a	a	a
12208	6.17	9.98	a	a	a
Mean	6.09	9.66	14.60	31.81	48.34
S.D.	0.20	0.48	0.32	0.43	0.37

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
12301	5.95	9.54	15.73	33.35	48.38
12302	6.21	9.86	a	a	a
12303	5.62	9.02	15.04	32.61	50.15
12304	5.89	9.17	a	a	a
12305	5.91	9.36	a	a	a
12306	6.04	10.10	16.96	35.75	51.92
12307	6.17	9.87	16.04	33.69	50.49
12308	6.78	10.57	a	a	a
12309	5.91	10.09	a	a	a
Mean	6.05	9.73	15.94	33.85	50.24
S.D.	0.32	0.50	0.80	1.34	1.46
12401	5.91	7.73	a	a	a
12402	5.87	8.45	14.78	33.58	48.91
12403	5.38	8.35	14.37	31.41	47.22
12404	5.47	7.68	a	a	a
12405	5.53	8.17	14.17	30.95	47.27
12406	5.66	8.04	a	a	a
12407	5.34	7.55	a	a	a
12408	5.91	8.62	14.32	32.88	51.26
12409	5.71	8.44	a	a	a
12410	5.77	8.57	a	a	a
12414	5.39	7.88	a	a	a
Mean	5.63	8.13	14.41	32.21	48.67
S.D.	0.22	0.38	0.26	1.23	1.90
12501	6.35	10.59	18.62	38.00	56.39
12515	6.68	11.34	19.46	38.86	53.72
Mean	6.52	10.97	19.04	38.43	55.06
S.D.	0.23	0.53	0.59	0.61	1.89

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
12601	7.11	11.54	a	a	a
12602	7.07	12.22	a	a	a
12603	7.29	12.57	20.17	41.50	63.70
12604	7.08	12.31	20.34	39.92	64.03
12605	7.04	11.87	a	a	a
12606	7.46	12.36	19.56	39.74	62.97
12607	7.57	12.17	18.93	39.27	61.50
12613	6.35	11.15	a	a	a
Mean	7.12	12.02	19.75	40.11	63.05
S.D.	0.37	0.47	0.64	0.97	1.12
12701	6.84	9.99	15.41	32.66	52.67
12702	7.52	10.89	a	a	a
12703	6.96	10.16	a	a	a
12704	7.30	10.54	a	a	a
12705	7.56	11.14	17.46	35.65	55.69
12706	7.81	11.48	a	a	a
12707	7.83	11.09	17.06	34.60	55.26
12708	7.78	11.53	17.53	35.22	56.12
12709	7.49	10.42	a	a	a
Mean	7.45	10.80	16.87	34.53	54.94
S.D.	0.36	0.56	0.99	1.32	1.55
12801	6.75	11.14	a	a	a
12802	6.76	10.95	17.07	33.60	56.47
12803	5.58	9.59	15.12	32.04	50.85
12804	6.77	11.25	16.89	34.60	56.87
12805	6.88	10.92	a	a	a
12806	6.39	10.98	17.29	34.41	55.47
Mean	6.52	10.81	16.59	33.66	54.92
S.D.	0.49	0.61	1.00	1.17	2.77
12901	7.31	13.26	a	a	a
12902	7.02	12.09	20.39	42.71	66.03
12903	7.05	12.67	a	a	a
12904	6.83	12.25	20.99	42.99	63.27
12905	7.16	12.97	20.85	42.87	65.39
12906	6.82	12.71	21.12	43.55	64.27
12907	7.12	12.24	a	a	a
12914	6.60	11.88	a	a	a
Mean	6.99	12.51	20.84	43.03	64.74
S.D.	0.23	0.47	0.32	0.37	1.22

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
13001	6.90	12.03	19.56	38.04	59.07
13002	7.29	11.98	19.83	39.58	64.24
13003	7.36	12.98	a	a	a
13004	7.52	12.83	a	a	a
13005	6.78	11.94	a	a	a
13006	7.14	12.49	a	a	a
13007	7.01	11.14	18.48	37.19	60.81
13008	7.18	11.90	a	a	a
13009	6.88	12.52	20.17	38.53	62.61
Mean	7.12	12.20	19.51	38.34	61.68
S.D.	0.25	0.56	0.73	1.00	2.24
13101	7.45	11.19	18.25	38.58	56.61
13102	6.60	10.62	17.51	39.89	61.34
13103	6.62	10.58	17.29	38.73	58.83
Mean	6.89	10.80	17.68	39.07	58.93
S.D.	0.49	0.34	0.50	0.72	2.37
13201	7.08	11.93	a	a	a
13202	6.70	11.64	18.40	39.91	63.53
13203	6.81	13.06	21.65	44.37	69.83
13204	6.95	12.11	20.17	41.55	67.14
13205	7.13	12.38	20.21	41.59	64.85
13206	7.12	12.03	a	a	a
13207	7.09	12.34	a	a	a
Mean	6.98	12.21	20.11	41.86	66.34
S.D.	0.17	0.45	1.33	1.85	2.77
13301	6.60	10.78	17.04	33.98	53.14
13302	7.19	11.53	18.43	36.78	60.34
13303	6.68	10.81	16.95	33.45	54.40
Mean	6.82	11.04	17.47	34.74	55.96
S.D.	0.32	0.42	0.83	1.79	3.85
13401	6.77	10.36	15.50	29.82	49.02
13402	7.68	11.21	16.60	33.09	52.58
13403	7.48	11.29	17.08	33.06	55.70
Mean	7.31	10.95	16.39	31.99	52.43
S.D.	0.48	0.52	0.81	1.88	3.34

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
13501	6.95	12.90	19.58	36.85	60.20
13502	6.98	12.37	18.35	34.42	58.96
13503	6.92	12.09	18.14	35.22	60.78
13504	7.12	12.08	18.46	34.88	56.45
Mean	6.99	12.36	18.63	35.34	59.10
S.D.	0.09	0.38	0.65	1.06	1.92
13601	7.08	11.43	17.20	32.80	50.98
13602	7.32	11.93	18.52	33.78	53.83
13603	6.45	10.00	15.02	28.51	42.79
13604	7.56	12.29	a	a	a
13605	6.92	11.93	17.95	32.16	50.63
Mean	7.07	11.52	17.17	31.81	49.56
S.D.	0.42	0.90	1.53	2.30	4.73
13701	6.67	11.02	a	a	a
13702	6.97	11.15	a	a	a
13703	6.58	10.69	a	a	a
13704	6.06	9.39	a	a	a
13705	6.22	10.48	16.89	34.56	48.19
13706	6.73	10.34	16.88	34.12	51.69
13707	6.56	10.65	a	a	a
13708	6.72	10.89	17.47	33.11	48.57
13709	6.68	11.08	17.97	35.20	51.66
13710	7.19	10.62	a	a	a
13712	6.79	11.16	a	a	a
Mean	6.65	10.68	17.30	34.25	50.03
S.D.	0.31	0.51	0.52	0.88	1.91
13801	c	10.63	a	a	a
13802	c	11.55	18.37	34.84	55.59
13803	c	10.81	17.84	33.58	54.84
13804	c	10.89	a	a	a
13805	c	11.22	a	a	a
13806	c	11.41	17.93	32.26	52.84
13807	c	10.98	17.78	34.30	56.19
13808	c	11.41	a	a	a
Mean		11.11	17.98	33.75	54.87
S.D.		0.33	0.27	1.12	1.46

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
13901	6.90	11.69	18.65	36.39	57.25
13902	6.48	10.86	16.87	34.42	53.54
13903	6.29	10.71	16.82	34.13	54.64
13904	6.79	11.18	17.75	33.86	54.64
13905	6.37	10.92	a	a	a
13906	6.24	10.35	a	a	a
Mean	6.51	10.95	17.52	34.70	55.02
S.D.	0.27	0.45	0.86	1.15	1.58
14001	6.39	10.24	15.16	30.98	47.65
14002	6.52	10.42	15.37	31.91	50.58
14003	6.17	9.73	a	a	a
14004	6.16	9.92	14.88	31.95	49.21
14005	6.15	10.04	a	a	a
14006	6.30	10.27	15.91	32.59	52.89
Mean	6.28	10.10	15.33	31.86	50.08
S.D.	0.15	0.25	0.44	0.66	2.22
14101	7.58	12.29	a	a	a
14102	7.47	11.51	a	a	a
14103	6.82	11.15	a	a	a
14104	7.10	11.81	17.46	37.22	53.57
14105	7.29	12.36	19.66	39.43	56.55
14106	6.92	11.99	a	a	a
14107	7.43	11.71	19.35	40.39	59.42
14108	7.78	12.90	a	a	a
14109	7.35	12.45	19.67	40.31	60.68
14110	6.73	11.18	a	a	a
Mean	7.25	11.94	19.04	39.34	57.56
S.D.	0.34	0.57	1.06	1.48	3.17
14200	5.77	8.89	a	a	a
14201	5.46	8.44	14.54	32.61	49.51
14202	6.05	9.55	a	a	a
14203	5.11	8.10	a	a	a
14204	5.64	9.01	a	a	a
14205	5.49	8.86	a	a	a
14206	5.73	8.99	15.23	33.62	50.46
14207	5.75	9.31	16.36	36.59	54.74
14208	6.19	9.68	16.53	34.79	51.22
14209	5.57	8.90	a	a	a
14210	5.79	9.35	a	a	a
Mean	5.69	9.01	15.67	34.40	51.48
S.D.	0.29	0.46	0.95	1.71	2.28

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
14301	6.81	10.75	16.75	34.27	56.38
14302	6.87	11.18	17.43	34.82	56.38
14303	5.92	9.91	15.61	32.84	54.39
14304	6.86	10.06	15.29	32.85	51.96
14313	6.81	10.83	a	a	a
Mean	6.65	10.55	16.27	33.70	54.78
S.D.	0.41	0.54	1.00	1.01	2.10
14401	7.32	9.54	14.86	31.02	50.49
14402	6.97	9.16	14.60	30.55	51.22
14403	6.77	9.41	14.64	29.71	48.64
14404	7.11	9.56	14.27	29.52	46.86
14405	6.74	9.49	a	a	a
Mean	6.98	9.43	14.59	30.20	49.30
S.D.	0.24	0.16	0.24	0.71	1.96
14501	6.00	10.03	14.74	28.73	38.19
14502	6.00	9.87	14.65	29.55	39.59
14503	5.90	10.07	15.25	29.71	41.03
14504	6.21	9.47	14.42	29.13	38.77
Mean	6.03	9.86	14.77	29.28	39.40
S.D.	0.13	0.27	0.35	0.44	1.23
14601	6.28	10.01	16.22	36.23	57.13
14603	6.11	9.82	15.51	35.58	54.96
14604	5.79	9.26	14.98	32.90	48.71
14605	6.65	10.15	16.45	36.72	56.22
14611	6.01	9.69	a	a	a
14616	5.66	9.13	a	a	a
Mean	6.08	9.68	15.79	35.36	54.26
S.D.	0.36	0.41	0.67	1.70	3.80
14701	5.37	8.67	a	a	a
14702	5.90	10.09	15.86	32.23	49.63
14703	5.57	9.18	14.67	30.42	46.98
14704	5.78	8.82	14.54	31.74	49.66
14705	5.63	7.32	12.21	28.84	42.92
14706	5.35	8.71	a	a	a
14707	6.03	9.29	a	a	a
Mean	5.66	8.87	14.32	30.81	47.30
S.D.	0.26	0.84	1.53	1.52	3.18

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
2 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
14801	6.72	11.33	17.33	33.78	53.64
14802	6.47	10.81	a	a	a
14803	6.54	10.90	17.57	34.24	56.15
14804	5.88	9.28	14.86	30.42	49.72
14805	6.44	10.90	17.04	33.63	55.47
Mean	6.41	10.64	16.70	33.02	53.75
S.D.	0.32	0.79	1.25	1.75	2.89
14901	6.33	11.69	17.36	30.70	45.46
14902	6.39	11.72	16.40	37.77	57.10
14903	6.21	11.08	17.84	38.93	60.14
Mean	6.31	11.50	17.20	35.80	54.23
S.D.	0.09	0.36	0.73	4.45	7.75
15001	7.03	11.20	16.59	31.93	51.98
15002	6.87	11.65	18.21	35.42	54.05
15003	6.77	11.13	16.86	34.42	54.34
15004	7.45	11.90	18.08	34.03	52.50
15005	6.79	10.81	a	a	a
15015	6.69	11.39	15.83	30.77	47.54
Mean	6.93	11.35	17.11	33.31	52.08
S.D.	0.28	0.39	1.02	1.91	2.73

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
15101	7.56	12.53	20.10	40.10	65.02
15102	7.46	12.22	a	a	a
15103	7.06	12.40	19.94	39.47	62.87
15104	6.92	11.69	18.44	37.60	60.21
15105	7.10	11.87	18.80	37.86	62.27
15106	6.44	11.56	a	a	a
Mean	7.09	12.05	19.32	38.76	62.59
S.D.	0.40	0.40	0.82	1.22	1.98
15201	6.12	9.75	15.55	34.31	56.34
15202	6.28	10.53	a	a	a
15203	6.37	10.43	16.54	35.36	56.63
15204	6.20	10.04	16.19	34.58	53.70
15205	6.93	10.39	a	a	a
15206	6.47	10.56	a	a	a
15207	6.63	10.73	a	a	a
15208	7.02	11.17	18.14	37.53	59.66
Mean	6.50	10.45	16.61	35.45	56.58
S.D.	0.33	0.43	1.10	1.46	2.44
15301	7.16	11.56	17.66	34.66	54.67
15302	6.87	10.99	16.93	33.43	53.62
15303	6.88	10.55	16.00	33.16	53.56
15304	6.85	10.52	15.87	33.46	51.86
15305	7.30	11.93	a	a	a
Mean	7.01	11.11	16.62	33.68	53.43
S.D.	0.21	0.62	0.84	0.67	1.16
15401	6.56	11.06	17.05	34.49	54.89
15402	6.55	10.87	17.09	34.80	57.71
15403	6.04	9.67	a	a	a
15404	6.54	10.83	17.18	35.28	55.30
15405	5.98	10.23	16.53	34.27	53.95
15406	6.30	9.90	a	a	a
15407	6.99	10.70	a	a	a
Mean	6.42	10.47	16.96	34.71	55.46
S.D.	0.35	0.53	0.29	0.44	1.60

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
15501	6.20	9.54	a	a	a
15502	6.45	10.90	17.44	36.42	59.05
15503	6.78	10.07	a	a	a
15504	6.45	10.26	16.18	35.58	61.23
15505	6.23	9.78	16.53	36.49	58.03
15506	6.78	10.57	16.82	36.65	59.68
Mean	6.48	10.19	16.74	36.29	59.50
S.D.	0.25	0.50	0.53	0.48	1.34
15601	6.07	8.76	14.55	32.48	52.84
15602	6.52	10.20	a	a	a
15603	6.16	9.68	a	a	a
15604	6.35	10.34	17.11	35.00	57.39
15605	7.02	11.11	a	a	a
15606	6.92	10.17	16.87	35.98	57.15
15607	6.39	9.76	16.38	34.70	54.70
15608	6.62	10.00	a	a	a
Mean	6.51	10.00	16.23	34.54	55.52
S.D.	0.34	0.67	1.16	1.48	2.16
15701	7.06	11.09	17.85	35.64	58.73
15702	7.00	10.92	16.82	34.88	56.74
15703	6.26	10.11	a	a	a
15704	6.86	10.61	16.79	33.35	53.48
15705	6.75	10.52	a	a	a
15706	7.12	11.45	18.09	37.43	58.64
Mean	6.84	10.78	17.39	35.33	56.90
S.D.	0.32	0.47	0.68	1.70	2.46
15801	6.40	10.25	15.57	31.85	51.55
15802	5.81	9.54	a	a	a
15803	5.68	8.95	14.67	30.04	48.65
15804	5.82	9.18	14.79	30.80	49.02
15805	5.75	9.56	15.58	31.30	49.22
15806	3.19	b	b	b	b
15811	5.71	9.41	a	a	a
Mean	5.48	9.48	15.15	31.00	49.61
S.D.	1.04	0.44	0.49	0.77	1.31

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
16001	6.37	10.05	a	a	a
16002	6.85	10.64	a	a	a
16003	6.38	10.34	16.25	32.90	49.03
16004	6.58	10.94	17.16	33.34	55.38
16005	6.76	7.32	16.99	33.68	53.99
16006	6.18	9.85	a	a	a
16007	6.06	10.14	15.67	32.76	51.35
Mean	6.45	9.90	16.52	33.17	52.44
S.D.	0.29	1.19	0.69	0.42	2.82
16101	6.42	10.85	16.79	32.00	49.54
16102	5.71	9.07	14.13	28.02	43.41
16103	6.51	10.31	15.86	30.92	48.09
16104	5.81	9.79	15.57	31.31	50.66
16105	6.76	11.05	a	a	a
16106	5.93	10.22	a	a	a
16107	6.01	9.91	a	a	a
Mean	6.16	10.17	15.59	30.56	47.93
S.D.	0.40	0.67	1.10	1.75	3.19
16202	7.10	12.48	18.91	37.97	56.93
16203	6.69	10.91	17.10	34.32	51.66
16204	6.54	11.37	18.01	34.78	50.72
16205	6.77	12.29	19.42	37.97	58.71
Mean	6.78	11.76	18.36	36.26	54.51
S.D.	0.24	0.75	1.02	1.98	3.92
16301	6.79	10.57	17.00	34.16	53.33
16302	6.44	9.84	a	a	a
16303	6.08	9.49	a	a	a
16304	6.92	11.20	17.22	34.12	53.03
16305	6.69	10.35	16.61	33.16	54.21
16306	5.31	8.34	13.51	30.05	47.47
Mean	6.37	9.97	16.09	32.87	52.01
S.D.	0.60	0.99	1.74	1.94	3.07

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
16401	6.46	10.28	a	a	a
16402	6.32	9.11	14.12	32.20	47.07
16403	4.96	b	b	b	b
16404	6.13	9.69	14.96	32.51	49.20
16405	5.97	9.76	a	a	a
16406	6.18	9.29	14.52	32.56	48.21
16407	6.17	9.62	14.62	32.53	48.81
Mean	6.03	9.63	14.56	32.45	48.32
S.D.	0.49	0.41	0.35	0.17	0.93
16501	5.99	9.53	a	a	a
16502	6.09	9.76	14.17	32.18	53.31
16503	6.54	b	b	b	b
16504	5.64	8.53	13.89	32.83	51.86
16505	6.60	10.38	16.26	35.00	57.23
16506	5.89	9.13	a	a	a
16507	5.85	9.32	a	a	a
16508	6.29	10.27	15.81	34.22	56.62
Mean	6.11	9.56	15.03	33.56	54.76
S.D.	0.34	0.65	1.18	1.28	2.59
16601	5.58	9.06	14.77	31.66	49.61
16602	5.75	9.44	15.41	32.56	51.02
16603	5.71	9.34	a	a	a
16604	5.64	9.16	14.76	31.03	50.53
16605	5.48	9.12	14.65	31.33	48.70
Mean	5.63	9.22	14.90	31.65	49.97
S.D.	0.11	0.16	0.35	0.66	1.03
16701	5.13	8.91	13.84	31.31	47.01
16702	5.86	9.84	15.58	32.66	50.12
16703	6.08	10.49	16.78	35.10	54.01
16704	5.75	9.84	15.55	33.39	48.21
16705	5.65	9.91	a	a	a
16706	5.94	10.06	a	a	a
Mean	5.74	9.84	15.44	33.12	49.84
S.D.	0.33	0.52	1.21	1.58	3.06

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
16801	6.58	9.55	15.66	33.92	52.53
16802	6.46	9.75	a	a	a
16803	6.66	9.82	a	a	a
16804	6.19	9.14	a	a	a
16805	6.61	10.18	16.48	34.32	53.29
16806	6.11	9.83	a	a	a
16807	6.43	9.52	15.45	33.26	52.80
16808	6.13	9.14	a	a	a
16809	6.12	9.50	15.76	33.46	52.35
Mean	6.37	9.60	15.84	33.74	52.74
S.D.	0.23	0.34	0.45	0.48	0.41
16901	6.15	10.50	15.84	31.40	48.23
16902	6.08	10.22	15.28	31.48	48.23
16903	6.14	10.68	15.08	33.51	51.77
16904	5.74	10.03	a	a	a
16905	5.69	9.68	14.96	31.17	47.90
Mean	5.96	10.22	15.29	31.89	49.03
S.D.	0.23	0.39	0.39	1.09	1.83
17001	6.26	8.98	a	a	a
17002	6.25	8.97	a	a	a
17003	5.95	9.15	a	a	a
17004	5.78	9.46	16.07	34.77	57.66
17005	5.75	8.05	13.24	31.84	51.88
17006	6.04	8.98	14.46	33.47	54.87
17007	6.34	10.31	16.45	35.63	58.78
Mean	6.05	9.13	15.06	33.93	55.80
S.D.	0.24	0.68	1.49	1.65	3.09
17101	6.57	10.46	a	a	a
17102	6.87	10.59	16.17	32.32	51.91
17103	6.51	10.19	a	a	a
17104	6.09	9.78	15.46	31.77	51.29
17105	6.57	10.71	16.64	34.06	55.35
17106	6.27	10.08	15.87	33.15	53.39
Mean	6.48	10.30	16.04	32.83	52.99
S.D.	0.27	0.35	0.50	1.00	1.81

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
17201	5.78	7.93	a	a	a
17202	5.60	7.79	a	a	a
17203	6.43	8.95	13.98	31.89	48.65
17204	5.78	8.33	a	a	a
17205	5.21	7.11	a	a	a
17206	5.97	8.26	12.53	29.20	46.33
17207	6.14	8.47	13.38	31.11	48.62
17208	5.88	7.78	12.13	28.63	43.00
17209	5.41	7.84	a	a	a
Mean	5.80	8.05	13.01	30.21	46.65
S.D.	0.37	0.52	0.83	1.54	2.66
17301	6.91	b	b	b	b
17302	7.94	12.97	a	a	a
17303	7.56	12.97	21.09	40.10	61.93
17304	7.94	12.86	20.88	40.42	63.05
17305	7.81	13.11	21.30	40.66	60.73
17306	8.18	13.28	a	a	a
17307	8.02	13.25	21.28	41.95	60.76
17308	8.13	11.86	a	a	a
Mean	7.81	12.90	21.14	40.78	61.62
S.D.	0.41	0.48	0.20	0.81	1.11
17401	6.82	11.51	18.40	38.58	61.62
17402	6.92	11.92	19.35	40.56	64.64
17403	7.39	11.83	18.85	39.38	62.98
17404	6.94	11.64	a	a	a
17405	7.24	11.73	a	a	a
17406	7.16	12.08	19.01	38.51	60.91
Mean	7.08	11.79	18.90	39.26	62.54
S.D.	0.22	0.20	0.39	0.95	1.64
17501	6.46	9.09	14.61	30.16	46.76
17502	6.69	9.48	15.01	30.13	47.98
17503	6.84	9.86	a	a	a
17504	6.81	9.01	13.63	29.53	45.71
17505	6.60	8.42	13.24	28.25	43.45
Mean	6.68	9.17	14.12	29.52	45.98
S.D.	0.16	0.54	0.83	0.89	1.92

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
17601	6.51	11.53	17.56	33.82	52.44
17602	6.11	10.73	16.72	32.76	50.19
17603	6.34	10.83	16.88	32.30	50.36
17604	6.10	10.96	17.03	32.25	53.18
17605	6.49	11.05	a	a	a
17613	6.45	11.52	a	a	a
Mean	6.33	11.10	17.05	32.78	51.54
S.D.	0.19	0.34	0.36	0.73	1.50
17701	6.04	9.59	14.26	27.43	48.08
17702	6.54	10.31	15.67	28.62	48.98
17703	6.22	9.26	15.12	29.04	49.13
17704	6.07	9.73	14.49	26.84	45.96
Mean	6.22	9.72	14.89	27.98	48.04
S.D.	0.23	0.44	0.64	1.02	1.46
17801	6.49	10.41	16.00	28.98	48.42
17802	7.07	10.29	15.39	26.98	45.49
17803	6.27	9.45	15.12	26.98	45.50
Mean	6.61	10.05	15.50	27.65	46.47
S.D.	0.41	0.52	0.45	1.15	1.69
17901	6.91	10.68	16.48	32.58	54.98
17902	6.61	10.21	15.57	32.11	53.09
17903	5.95	9.74	15.12	31.82	51.71
17904	6.48	10.34	a	a	a
17905	6.49	10.46	16.17	33.21	52.35
17906	6.68	10.38	a	a	a
17907	6.30	9.59	a	a	a
17908	6.33	9.74	a	a	a
Mean	6.47	10.14	15.84	32.43	53.03
S.D.	0.29	0.40	0.61	0.61	1.42
18001	5.86	8.85	13.81	26.86	45.59
18002	6.04	9.09	a	a	a
18003	6.16	9.40	a	a	a
18004	5.69	8.63	13.43	25.11	42.68
18005	5.82	9.22	a	a	a
18006	6.28	9.23	14.12	26.59	43.21
18007	5.94	9.09	13.71	25.50	42.07
Mean	5.98	9.07	13.79	26.19	43.83
S.D.	0.22	0.28	0.35	0.94	1.55

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
18101	6.94	10.29	15.63	30.00	49.51
18102	7.00	10.40	15.50	30.19	51.15
18103	6.09	10.08	15.01	30.11	50.07
18104	6.82	10.38	15.46	29.79	48.89
Mean	6.71	10.29	15.40	30.02	49.90
S.D.	0.42	0.15	0.27	0.17	0.96
18201	6.30	9.49	13.81	28.34	46.22
18202	6.16	9.56	13.88	29.13	48.12
18203	6.40	9.89	14.53	29.36	48.57
18204	6.23	9.46	13.99	28.50	48.67
Mean	6.27	9.60	14.05	28.83	47.90
S.D.	0.10	0.20	0.33	0.49	1.14
18301	5.94	9.85	16.58	34.05	55.01
18302	6.82	10.72	a	a	a
18303	6.52	10.89	17.22	34.61	55.11
18304	6.48	9.28	a	a	a
18305	7.01	10.25	17.58	35.49	57.49
18306	6.72	10.98	18.10	35.96	57.93
Mean	6.58	10.33	17.37	35.03	56.39
S.D.	0.37	0.67	0.64	0.86	1.54
18401	6.06	9.77	a	a	a
18402	6.35	9.92	a	a	a
18403	6.40	9.24	13.84	26.33	45.92
18404	6.26	9.87	12.74	26.84	44.32
18405	5.88	9.25	14.06	28.23	46.96
18406	5.78	9.46	14.07	28.80	47.28
18407	6.27	9.95	a	a	a
Mean	6.14	9.64	13.68	27.55	46.12
S.D.	0.24	0.31	0.63	1.16	1.33
18501	7.03	10.41	15.13	28.14	51.38
18502	6.53	10.85	15.94	29.16	48.33
18503	7.38	11.73	17.13	31.13	52.80
18505	6.59	10.54	16.15	30.16	50.35
18514	6.79	10.48	a	a	a
Mean	6.86	10.80	16.09	29.65	50.72
S.D.	0.35	0.55	0.82	1.29	1.88

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
18601	6.35	9.51	14.94	28.35	43.73
18602	6.45	9.66	a	a	a
18603	5.89	8.97	13.96	27.46	42.30
18604	5.85	9.29	14.19	28.68	44.05
18605	5.60	8.91	12.95	25.42	38.02
Mean	6.03	9.27	14.01	27.48	42.03
S.D.	0.36	0.33	0.82	1.47	2.78
18701	6.66	10.30	a	a	a
18702	6.70	10.72	16.33	29.99	48.56
18703	6.61	10.49	15.48	28.91	50.40
18704	6.97	11.06	a	a	a
18705	6.31	10.22	15.52	28.13	44.43
18706	6.69	10.62	15.81	29.36	46.77
Mean	6.66	10.57	15.79	29.10	47.54
S.D.	0.21	0.31	0.39	0.78	2.55
18801	7.21	10.67	a	a	a
18802	6.48	10.44	16.85	31.92	53.86
18803	7.25	10.29	16.71	31.08	50.03
18804	5.94	9.00	a	a	a
18805	6.46	9.55	a	a	a
18806	6.54	9.94	a	a	a
18807	6.29	9.99	15.75	32.05	49.59
18808	6.86	10.48	16.27	31.93	51.82
Mean	6.63	10.05	16.40	31.75	51.33
S.D.	0.45	0.55	0.50	0.45	1.95
18901	5.33	7.80	a	a	a
18902	4.97	7.28	11.40	23.42	34.23
18903	5.11	7.72	a	a	a
18904	5.01	7.82	12.20	27.26	43.85
18905	5.16	7.50	a	a	a
18906	5.49	7.64	a	a	a
18907	5.16	7.90	12.29	24.93	40.27
18908	5.26	8.10	12.85	27.02	42.87
18909	4.84	6.56	a	a	a
Mean	5.15	7.59	12.19	25.66	40.31
S.D.	0.20	0.45	0.60	1.82	4.32

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
19001	6.07	7.75	11.97	25.30	42.68
19002	6.09	7.32	11.13	24.38	41.61
19003	5.44	b	b	b	b
19004	5.86	7.52	11.99	26.61	42.96
Mean	5.87	7.53	11.70	25.43	42.42
S.D.	0.30	0.22	0.49	1.12	0.71
19101	6.42	9.93	a	a	a
19102	6.18	10.15	14.74	29.94	47.79
19103	5.89	9.66	a	a	a
19104	6.12	9.17	14.51	28.97	43.78
19105	6.23	10.22	a	a	a
19106	5.26	9.82	15.30	30.61	49.13
19107	6.10	10.02	15.38	30.74	48.18
Mean	6.03	9.85	14.98	30.07	47.22
S.D.	0.37	0.36	0.42	0.81	2.36
19201	5.90	9.10	12.16	24.65	41.28
19202	5.86	8.26	11.57	23.81	37.91
19203	4.16	b	b	b	b
19204	5.47	8.43	11.68	24.27	40.34
19205	5.96	8.59	12.35	25.57	41.56
19206	5.62	8.25	a	a	a
19207	5.62	8.63	a	a	a
19208	5.82	8.40	a	a	a
Mean	5.55	8.52	11.94	24.58	40.27
S.D.	0.59	0.29	0.37	0.75	1.66
19301	5.85	8.82	14.03	30.18	45.82
19302	5.96	8.31	a	a	a
19303	5.14	7.81	12.78	27.74	43.54
19304	5.59	7.88	12.63	28.23	41.99
19306	5.39	7.66	12.50	27.52	41.42
19307	5.78	b	b	b	b
Mean	5.62	8.10	12.99	28.42	43.19
S.D.	0.31	0.47	0.71	1.21	1.97

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
19401	5.88	8.74	13.80	31.01	50.90
19402	6.52	9.27	14.98	32.69	55.18
19403	6.07	9.07	14.89	32.14	51.73
19404	6.20	9.24	14.11	30.19	49.80
19406	6.21	b	b	b	b
Mean	6.18	9.08	14.45	31.51	51.90
S.D.	0.23	0.24	0.58	1.12	2.32
19501	6.14	8.69	14.20	28.61	45.21
19502	5.91	8.63	13.35	27.82	43.76
19503	6.26	9.22	14.16	28.97	45.73
19504	6.27	9.04	a	a	a
19505	6.53	9.31	a	a	a
19506	5.99	9.09	14.92	30.57	47.28
19507	6.25	9.04	a	a	a
Mean	6.19	9.00	14.16	28.99	45.50
S.D.	0.20	0.25	0.64	1.16	1.45
19601	6.17	9.23	a	a	a
19602	6.45	9.72	14.56	26.07	44.69
19603	5.65	8.90	a	a	a
19604	5.97	9.41	14.15	25.44	44.83
19605	5.08	8.04	12.50	24.07	40.57
19606	5.73	8.80	13.01	24.73	42.39
Mean	5.84	9.02	13.56	25.08	43.12
S.D.	0.47	0.58	0.96	0.87	2.04
19701	6.46	8.51	12.78	25.81	41.51
19702	6.61	8.97	13.45	26.28	43.17
19703	6.13	7.57	11.56	24.87	38.62
19704	5.83	7.92	12.22	24.53	38.88
19705	6.42	8.71	a	a	a
Mean	6.29	8.34	12.50	25.37	40.55
S.D.	0.31	0.58	0.80	0.81	2.18

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Male)
18 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
19801	6.59	9.27	14.75	27.41	45.06
19802	6.81	9.97	15.84	28.79	47.40
19803	6.17	9.46	a	a	a
19804	7.04	10.10	a	a	a
19805	7.11	10.40	16.04	29.12	47.94
19806	6.75	10.21	a	a	a
19807	6.91	10.10	a	a	a
19808	7.27	10.48	16.10	29.33	48.75
Mean	6.83	10.00	15.68	28.66	47.29
S.D.	0.34	0.43	0.63	0.86	1.59
19901	4.95	7.01	10.90	23.60	37.80
19902	5.17	6.75	9.98	22.92	35.92
19903	5.55	7.51	11.31	25.24	40.69
19904	5.12	7.33	a	a	a
19905	5.56	7.50	11.51	24.85	39.67
19913	5.20	6.95	a	a	a
Mean	5.26	7.18	10.93	24.15	38.52
S.D.	0.25	0.32	0.68	1.08	2.11
20001	6.58	10.08	a	a	a
20002	6.38	9.22	15.27	30.52	51.90
20003	6.95	11.28	a	a	a
20004	6.82	10.05	15.44	30.43	51.06
20005	6.41	9.50	14.83	30.70	50.52
20006	6.31	9.88	a	a	a
20007	6.14	9.56	a	a	a
20008	6.04	9.35	15.14	30.59	50.11
Mean	6.45	9.87	15.17	30.56	50.90
S.D.	0.31	0.65	0.26	0.11	0.77

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
10111	6.56	10.47	a	a	a
10112	6.32	11.01	17.10	33.50	55.35
10113	6.56	11.44	17.93	33.14	57.55
10114	6.61	11.33	a	a	a
10115	6.77	11.51	17.80	35.32	55.82
10116	6.58	10.81	a	a	a
10117	6.47	11.01	17.44	34.97	54.43
Mean	6.55	11.08	17.57	34.23	55.79
S.D.	0.14	0.37	0.37	1.07	1.31
10214	6.00	10.49	16.53	33.24	55.23
10215	6.96	11.52	17.15	34.43	55.25
10216	6.35	10.58	a	a	a
10217	6.03	10.24	15.83	33.52	57.13
10218	6.22	10.25	15.83	33.56	53.84
10219	6.36	10.94	a	a	a
Mean	6.32	10.67	16.34	33.69	55.36
S.D.	0.35	0.49	0.64	0.52	1.35
10311	6.51	11.55	a	a	a
10312	6.17	10.02	17.09	36.45	56.19
10313	6.42	11.05	18.22	37.15	58.72
10314	6.54	b	b	b	b
10315	6.17	10.89	18.03	37.17	56.83
10316	6.65	11.04	a	a	a
10317	6.10	10.53	a	a	a
10318	6.12	10.75	18.32	38.23	58.83
Mean	6.34	10.83	17.92	37.25	57.64
S.D.	0.22	0.48	0.56	0.73	1.33
10411	6.56	11.20	16.91	37.17	54.84
10412	6.95	12.23	19.07	39.31	58.72
10413	6.64	11.21	17.26	35.30	54.09
10414	6.46	11.01	a	a	a
10415	6.53	11.43	17.54	35.64	55.11
Mean	6.63	11.42	17.70	36.86	55.69
S.D.	0.19	0.48	0.95	1.83	2.07
10511	7.06	10.78	17.66	36.76	55.44
10512	6.39	10.30	16.73	34.66	52.92
10513	6.34	9.78	16.50	34.26	50.53
Mean	6.60	10.29	16.96	35.23	52.96
S.D.	0.40	0.50	0.61	1.34	2.46

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
10611	5.95	10.19	16.36	34.85	52.70
10612	5.74	10.44	a	a	a
10613	5.55	10.42	a	a	a
10614	6.38	11.49	18.03	37.16	59.37
10615	4.91	9.72	15.44	33.43	51.60
10616	5.79	10.82	17.69	36.94	58.16
Mean	5.72	10.51	16.88	35.60	55.46
S.D.	0.49	0.60	1.20	1.78	3.88
10711	6.60	12.20	17.81	36.68	54.87
10712	6.61	12.67	17.92	35.51	54.26
10713	5.87	10.95	16.64	34.86	52.01
10714	6.79	12.26	17.99	34.81	55.38
Mean	6.47	12.02	17.59	35.47	54.13
S.D.	0.41	0.74	0.64	0.87	1.49
10811	7.22	11.47	17.44	34.20	59.29
10812	6.71	11.08	a	a	a
10813	7.17	11.57	17.80	34.50	56.92
10814	6.77	11.51	a	a	a
10815	6.91	11.34	17.51	34.15	55.73
10816	6.18	10.71	16.37	32.36	52.15
Mean	6.83	11.28	17.28	33.80	56.02
S.D.	0.38	0.33	0.63	0.97	2.98
10911	6.59	11.15	17.76	34.71	52.69
Mean	6.59	11.15	17.76	34.71	52.69
S.D.	0.00	0.00	0.00	0.00	0.00
11011	6.73	10.88	17.71	35.88	54.51
11012	6.08	9.27	16.00	33.88	51.26
11013	6.15	10.40	a	a	a
11014	7.03	11.10	18.10	35.73	55.30
11015	6.72	9.61	16.31	34.49	53.65
11016	6.74	11.55	a	a	a
Mean	6.58	10.47	17.03	35.00	53.68
S.D.	0.38	0.88	1.03	0.97	1.75

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

Preweaning Period: Individual Pup Body Weights (Female)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
11111	7.16	11.82	18.35	35.85	56.46
11112	5.87	11.18	a	a	a
11113	6.52	9.74	15.29	30.32	46.09
11114	7.63	12.50	a	a	a
11115	6.85	11.50	a	a	a
11116	6.80	11.45	17.51	33.73	53.35
11117	7.21	11.94	17.63	32.33	50.50
Mean	6.86	11.45	17.20	33.06	51.60
S.D.	0.56	0.86	1.32	2.33	4.41
11211	6.40	10.28	16.73	35.04	54.32
11212	6.23	8.58	13.28	30.09	48.16
11213	6.24	10.58	17.46	34.54	54.47
Mean	6.29	9.81	15.82	33.22	52.32
S.D.	0.10	1.08	2.23	2.73	3.60
11311	6.03	10.44	17.64	35.13	55.73
11312	5.87	9.77	16.46	33.93	54.85
11314	6.22	10.49	a	a	a
11315	5.72	9.93	16.13	32.38	53.59
11316	6.11	10.55	17.00	33.74	55.42
Mean	5.99	10.24	16.81	33.80	54.90
S.D.	0.20	0.36	0.66	1.13	0.94
11411	5.63	8.86	14.39	32.34	50.19
11412	5.59	8.48	14.40	32.53	51.61
11413	6.16	9.68	16.14	34.84	57.00
11414	5.83	8.92	15.19	33.68	52.69
Mean	5.80	8.99	15.03	33.35	52.87
S.D.	0.26	0.50	0.83	1.16	2.94
11511	5.85	8.52	14.26	29.83	46.51
11512	5.39	8.91	a	a	a
11513	5.71	8.91	14.15	29.49	44.92
11514	5.55	8.69	13.66	28.71	42.83
11515	5.62	8.79	a	a	a
11516	5.46	7.99	a	a	a
11517	5.72	9.04	a	a	a
11518	5.62	8.85	a	a	a
11519	5.18	8.59	14.24	29.95	45.60
11504	5.85	8.64	a	a	a
Mean	5.60	8.69	14.08	29.50	44.97
S.D.	0.21	0.30	0.28	0.56	1.57

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
11611	6.29	10.78	17.09	34.28	56.23
11612	6.55	11.30	17.59	35.29	52.52
11613	6.68	11.23	a	a	a
11614	6.29	10.60	a	a	a
11615	6.82	11.39	17.77	33.03	52.14
11616	7.05	11.91	18.38	36.58	56.51
Mean	6.61	11.20	17.71	34.80	54.35
S.D.	0.30	0.47	0.53	1.51	2.34
11711	6.23	10.68	17.53	37.21	55.70
11712	6.21	8.29	14.52	33.88	52.94
Mean	6.22	9.49	16.03	35.55	54.32
S.D.	0.01	1.69	2.13	2.35	1.95
11811	6.44	11.64	17.74	39.36	59.61
11812	5.84	9.77	15.00	35.97	57.08
11813	5.87	11.04	16.91	37.01	56.34
11814	5.71	10.37	15.78	35.84	55.56
Mean	5.97	10.71	16.36	37.05	57.15
S.D.	0.32	0.81	1.21	1.63	1.76
11911	7.01	10.80	17.34	35.98	53.29
11912	6.11	9.94	a	a	a
11913	6.91	10.71	17.20	35.43	52.78
11914	6.99	10.95	17.58	36.04	55.48
11915	7.30	11.34	18.54	36.97	57.79
11916	7.26	11.83	a	a	a
11917	6.97	11.16	a	a	a
Mean	6.94	10.96	17.67	36.11	54.84
S.D.	0.39	0.59	0.60	0.64	2.29
12011	5.40	7.69	a	a	a
12012	5.78	8.62	13.52	29.21	47.06
12013	5.69	8.86	13.86	28.64	45.49
12014	5.37	8.26	a	a	a
12015	6.09	9.52	14.43	29.28	46.38
12016	6.07	9.86	15.31	31.30	50.95
12017	6.18	9.57	a	a	a
Mean	5.80	8.91	14.28	29.61	47.47
S.D.	0.33	0.79	0.78	1.16	2.41

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
0 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
12111	6.90	9.70	15.40	32.92	50.65
12112	5.98	10.16	a	a	a
12113	6.00	9.76	15.80	32.68	50.88
12114	6.34	9.47	16.31	33.59	51.81
12115	6.55	9.27	a	a	a
12116	5.94	10.12	a	a	a
12117	5.46	8.85	13.96	30.67	47.02
Mean	6.17	9.62	15.37	32.47	50.09
S.D.	0.47	0.47	1.01	1.26	2.11
12211	5.70	8.73	13.31	28.55	44.64
12212	5.89	8.91	13.43	30.66	46.13
12213	6.15	9.50	14.04	32.05	51.00
Mean	5.91	9.05	13.59	30.42	47.26
S.D.	0.23	0.40	0.39	1.76	3.33
12311	6.11	9.75	15.94	33.35	49.77
12312	5.97	9.86	16.14	33.06	48.75
12313	5.80	9.25	15.46	32.62	48.46
12314	5.78	9.00	14.70	31.41	47.39
Mean	5.92	9.47	15.56	32.61	48.59
S.D.	0.16	0.41	0.64	0.85	0.98
12411	4.88	6.72	11.91	29.10	42.90
12412	5.39	b	b	b	b
12413	5.34	7.04	12.17	29.22	42.03
12415	5.45	7.73	13.64	31.67	46.12
12416	5.24	8.07	13.76	29.82	44.68
Mean	5.26	7.39	12.87	29.95	43.93
S.D.	0.23	0.62	0.97	1.19	1.83
12511	6.21	9.80	17.12	36.44	58.74
12512	6.15	9.98	a	a	a
12513	6.15	10.13	a	a	a
12514	6.28	10.36	a	a	a
12516	6.19	9.78	a	a	a
12517	6.56	10.72	a	a	a
12518	4.79	8.42	14.78	33.45	49.94
12519	6.29	10.05	17.52	38.03	56.20
12520	6.69	10.74	18.43	37.44	55.71
12521	6.56	10.60	a	a	a
Mean	6.19	10.06	16.96	36.34	55.15
S.D.	0.53	0.68	1.55	2.04	3.72

a = Pup culled on day 4
b = Pup missing on day 4
c = Pup inadvertently culled on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
12611	7.16	11.28	17.99	37.65	59.18
12612	7.06	11.80	18.53	38.19	57.56
Mean	7.11	11.54	18.26	37.92	58.37
S.D.	0.07	0.37	0.38	0.38	1.15
12711	6.59	9.42	14.76	31.12	48.94
12712	7.28	10.04	15.82	32.51	48.63
12713	6.82	10.16	a	a	a
12714	6.90	10.36	a	a	a
12715	6.53	9.63	15.04	31.56	49.59
12716	6.66	9.85	15.58	32.82	51.30
Mean	6.80	9.91	15.30	32.00	49.62
S.D.	0.27	0.35	0.49	0.80	1.19
12811	6.34	10.64	16.53	32.90	53.33
12812	6.75	11.35	a	a	a
12813	6.43	11.16	17.53	33.56	55.97
12814	6.51	10.54	16.20	31.79	51.22
12815	6.51	10.94	16.85	34.26	53.88
Mean	6.51	10.93	16.78	33.13	53.60
S.D.	0.15	0.34	0.57	1.05	1.95
12911	6.85	11.89	19.72	40.33	60.36
12912	6.76	11.39	19.10	40.71	60.38
12913	6.64	11.15	18.61	38.50	55.13
Mean	6.75	11.48	19.14	39.85	58.62
S.D.	0.11	0.38	0.56	1.18	3.03
13011	6.55	11.54	18.53	37.70	58.28
13012	7.37	12.04	19.88	38.57	60.50
13013	6.95	11.49	18.82	38.47	62.74
13014	6.66	11.49	18.32	36.92	59.59
Mean	6.88	11.64	18.89	37.92	60.28
S.D.	0.37	0.27	0.69	0.77	1.88

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
13111	6.87	10.83	a	a	a
13112	7.12	11.09	a	a	a
13113	6.67	10.85	17.31	37.04	55.72
13114	6.58	10.67	17.51	37.97	56.28
13115	6.20	10.04	16.56	37.22	56.29
13116	6.46	10.30	a	a	a
13117	6.29	10.82	a	a	a
13118	6.39	10.50	a	a	a
13119	6.30	10.12	16.59	36.96	55.29
Mean	6.54	10.58	16.99	37.30	55.90
S.D.	0.30	0.36	0.49	0.46	0.48
13211	7.17	12.77	20.54	41.28	65.67
13212	6.78	12.17	20.28	41.65	63.76
13213	6.49	11.48	19.03	40.62	63.22
Mean	6.81	12.14	19.95	41.18	64.22
S.D.	0.34	0.65	0.81	0.52	1.29
13311	6.34	10.58	16.81	33.73	52.07
13312	6.47	10.57	a	a	a
13313	6.70	11.06	a	a	a
13314	6.33	10.96	a	a	a
13315	6.23	10.35	16.68	35.24	53.58
13316	6.52	11.05	a	a	a
13317	6.42	10.77	17.05	35.21	56.65
13318	5.37	9.38	14.95	31.58	50.54
Mean	6.30	10.59	16.37	33.94	53.21
S.D.	0.40	0.55	0.96	1.72	2.61
13411	7.37	11.15	a	a	a
13412	6.03	9.51	15.29	31.08	50.48
13413	6.84	10.04	15.46	30.57	51.83
13414	6.73	10.51	15.45	28.52	49.38
13415	6.99	10.70	a	a	a
13416	7.20	10.63	a	a	a
13417	6.79	12.29	15.54	30.07	53.81
13418	6.75	9.67	a	a	a
Mean	6.84	10.56	15.44	30.06	51.38
S.D.	0.40	0.89	0.10	1.11	1.91

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
13511	6.86	12.44	a	a	a
13512	6.75	11.65	17.67	35.23	56.16
13513	6.46	11.78	17.51	34.67	54.93
13514	6.51	12.09	17.87	34.11	54.72
13515	6.88	11.53	17.72	33.70	54.84
Mean	6.69	11.90	17.69	34.43	55.16
S.D.	0.20	0.37	0.15	0.67	0.67
13611	6.90	11.40	a	a	a
13612	7.06	11.99	18.47	34.51	54.95
13613	7.64	12.38	17.88	32.99	51.85
13614	7.14	11.85	17.12	32.21	48.81
13615	7.22	11.45	18.39	34.10	54.49
13616	7.34	12.14	a	a	a
Mean	7.22	11.87	17.97	33.45	52.53
S.D.	0.26	0.39	0.62	1.05	2.83
13711	6.00	9.78	15.53	32.04	44.50
13713	6.64	11.01	17.39	34.04	56.14
Mean	6.32	10.40	16.46	33.04	50.32
S.D.	0.45	0.87	1.32	1.41	8.23
13811	c	10.21	16.46	31.49	50.52
13812	c	10.79	17.29	33.95	55.80
13813	c	9.51	a	a	a
13814	c	9.57	15.60	31.07	49.87
13815	c	10.28	16.24	31.92	55.10
Mean		10.07	16.40	32.11	52.82
S.D.		0.54	0.70	1.28	3.06
13911	6.53	11.44	17.78	35.96	55.48
13912	6.10	10.70	16.80	33.32	51.92
13913	6.43	11.02	17.25	34.14	52.17
13914	6.10	10.47	a	a	a
13915	6.54	10.81	a	a	a
13916	6.04	8.98	14.60	29.87	48.42
Mean	6.29	10.57	16.61	33.32	52.00
S.D.	0.23	0.85	1.40	2.55	2.88

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
14011	5.93	9.25	14.80	31.73	48.71
14012	5.60	8.96	13.56	29.78	44.62
14013	6.39	9.93	a	a	a
14014	5.90	9.59	14.66	29.80	46.86
14015	5.93	9.04	13.94	29.84	45.82
Mean	5.95	9.35	14.24	30.29	46.50
S.D.	0.28	0.40	0.59	0.96	1.73
14111	6.39	10.44	16.27	34.14	51.33
14112	5.92	9.61	15.81	35.09	51.00
Mean	6.16	10.03	16.04	34.62	51.17
S.D.	0.33	0.59	0.33	0.67	0.23
14211	5.92	9.64	16.44	35.81	52.21
14212	5.43	8.32	13.84	30.92	46.41
14213	5.45	8.74	14.91	33.40	49.24
Mean	5.60	8.90	15.06	33.38	49.29
S.D.	0.28	0.67	1.31	2.45	2.90
14311	6.51	9.49	a	a	a
14312	6.40	9.75	a	a	a
14314	6.41	9.96	15.20	31.42	49.98
14315	6.01	9.71	15.16	31.13	49.38
14316	6.34	10.41	16.34	32.34	51.57
14317	5.50	8.56	13.80	29.86	46.89
Mean	6.20	9.65	15.13	31.19	49.46
S.D.	0.38	0.62	1.04	1.02	1.94
14411	6.54	8.43	a	a	a
14412	6.32	8.66	13.55	28.44	49.72
14413	6.46	9.17	a	a	a
14414	6.14	8.01	12.53	27.30	42.54
14415	6.49	9.55	a	a	a
14416	6.73	8.85	14.33	28.87	48.33
14417	6.24	8.94	13.51	28.20	46.59
14418	6.30	b	b	b	b
14419	6.70	8.58	a	a	a
Mean	6.44	8.77	13.48	28.20	46.80
S.D.	0.20	0.47	0.74	0.66	3.11

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
14511	5.53	9.03	13.76	26.66	37.04
14512	6.11	8.42	13.20	27.12	35.96
14513	5.71	8.99	a	a	a
14514	5.43	8.67	13.55	26.68	36.18
14515	5.74	9.03	a	a	a
14516	5.66	9.12	13.70	28.15	38.76
14517	5.47	9.05	a	a	a
Mean	5.66	8.90	13.55	27.15	36.99
S.D.	0.23	0.26	0.25	0.70	1.27
14611	6.01	9.69	a	a	a
14612	5.96	9.66	15.54	35.93	52.32
14613	6.00	9.58	15.36	33.16	51.11
14614	6.28	8.16	13.39	32.23	47.02
14615	5.81	8.88	14.57	33.12	50.91
14602	6.16	9.63	a	a	a
Mean	6.04	9.27	14.72	33.61	50.34
S.D.	0.16	0.62	0.98	1.61	2.30
14711	4.87	7.96	a	a	a
14712	4.87	8.38	13.83	30.39	47.73
14713	5.14	8.20	13.23	28.88	43.51
14714	5.30	8.35	14.36	30.49	45.10
14715	5.13	7.82	12.74	28.74	42.25
14716	5.19	8.15	a	a	a
14717	5.48	9.42	a	a	a
Mean	5.14	8.33	13.54	29.63	44.65
S.D.	0.22	0.52	0.71	0.94	2.36
14811	5.82	8.87	14.87	30.14	49.29
14812	5.89	9.91	15.88	32.14	52.49
14813	6.78	10.86	17.29	34.35	54.59
14814	5.75	9.65	a	a	a
14815	6.25	10.55	a	a	a
14816	5.92	10.61	17.28	32.91	50.84
Mean	6.07	10.08	16.33	32.39	51.80
S.D.	0.39	0.75	1.18	1.75	2.27

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

Preweaning Period: Individual Pup Body Weights (Female)
2 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
14911	6.62	11.70	a	a	a
14912	5.98	11.27	15.28	31.56	47.94
14913	6.41	11.07	17.72	35.26	55.49
14914	5.90	10.90	16.74	34.93	52.79
14915	6.00	10.86	a	a	a
14916	5.92	10.07	12.52	27.51	42.00
14917	6.08	b	b	b	b
Mean	6.13	10.98	15.57	32.32	49.56
S.D.	0.28	0.54	2.26	3.61	5.93
15011	6.54	10.65	15.87	31.20	46.92
15012	6.44	b	b	b	b
15013	6.27	10.37	15.99	31.37	48.87
15014	5.75	9.49	14.94	29.88	44.72
Mean	6.25	10.17	15.60	30.82	46.84
S.D.	0.35	0.61	0.57	0.82	2.08

a = Pup culled on day 4
b = Pup missing on day 4
c = Litter inadvertently not weighed on day 0

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
6 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
15111	7.01	11.62	18.70	38.11	60.34
15112	6.95	11.70	18.44	36.51	59.13
15113	6.63	11.50	a	a	a
15114	6.36	10.93	17.12	35.97	58.36
15115	6.82	11.88	18.22	36.49	60.25
Mean	6.75	11.53	18.12	36.77	59.52
S.D.	0.26	0.36	0.69	0.93	0.95
15211	5.94	9.20	14.81	32.74	52.96
15212	5.79	9.31	14.78	33.07	53.27
15213	5.69	9.56	14.84	32.95	52.33
15214	5.87	9.18	a	a	a
15215	6.40	10.04	16.57	36.13	54.29
Mean	5.94	9.46	15.25	33.72	53.21
S.D.	0.27	0.36	0.88	1.61	0.82
15311	6.74	10.83	16.77	32.99	51.76
15312	7.06	9.99	a	a	a
15313	6.62	11.23	16.96	34.15	53.77
15314	6.66	10.93	16.61	33.27	52.01
15315	6.87	11.13	16.45	33.64	55.60
Mean	6.79	10.82	16.70	33.51	53.29
S.D.	0.18	0.49	0.22	0.50	1.78
15411	6.21	10.29	a	a	a
15412	6.05	10.02	15.87	32.28	51.06
15413	6.07	10.23	16.48	33.89	52.78
15414	5.90	9.58	a	a	a
15415	5.33	9.04	14.47	30.03	47.20
15416	6.39	10.99	17.20	34.80	56.83
15417	6.23	10.63	a	a	a
Mean	6.03	10.11	16.01	32.75	51.97
S.D.	0.34	0.65	1.16	2.09	3.99
15511	6.16	10.09	16.66	34.67	55.68
15512	6.12	9.83	a	a	a
15513	6.35	9.88	16.14	34.00	55.54
15514	6.76	10.52	a	a	a
15515	6.32	9.26	15.20	32.12	51.49
15516	6.35	10.02	a	a	a
15517	6.21	9.78	a	a	a
15518	6.86	10.93	17.43	35.59	56.16
Mean	6.39	10.04	16.36	34.10	54.72
S.D.	0.27	0.50	0.94	1.47	2.17

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
6 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
15611	6.21	10.11	16.47	35.02	56.42
15612	6.04	9.06	a	a	a
15613	6.29	9.96	a	a	a
15614	6.24	9.81	16.49	34.42	53.33
15615	5.78	9.30	15.38	33.29	53.62
15616	6.33	10.57	a	a	a
15617	6.55	9.91	16.11	33.67	53.53
Mean	6.21	9.82	16.11	34.10	54.23
S.D.	0.24	0.50	0.52	0.77	1.47
15711	6.05	9.87	a	a	a
15712	6.55	10.40	16.86	34.56	54.13
15713	6.53	10.15	a	a	a
15714	6.62	9.99	16.54	34.68	53.91
15715	6.31	9.98	a	a	a
15716	6.58	10.14	16.09	34.34	54.48
15717	6.14	10.22	16.27	34.38	55.63
Mean	6.40	10.11	16.44	34.49	54.54
S.D.	0.23	0.18	0.34	0.16	0.77
15812	5.69	9.48	15.20	31.68	49.89
15813	5.71	9.29	14.34	30.21	46.87
15814	5.71	9.70	15.64	31.02	50.18
15815	5.59	9.11	a	a	a
15816	5.43	8.87	14.46	30.84	48.10
15817	5.46	8.99	a	a	a
Mean	5.60	9.24	14.91	30.94	48.76
S.D.	0.13	0.31	0.62	0.60	1.56
16011	5.90	9.61	14.97	32.00	50.70
16012	6.03	9.87	a	a	a
16013	6.31	10.31	15.37	32.30	51.72
16014	6.35	9.97	15.85	32.76	52.74
16015	5.91	10.11	15.76	32.48	51.79
Mean	6.10	9.97	15.49	32.39	51.74
S.D.	0.22	0.26	0.40	0.32	0.83

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
16111	6.09	9.91	15.74	29.70	48.54
16112	6.12	10.01	15.30	30.05	47.55
16113	5.33	8.61	13.66	27.70	43.01
16114	5.49	8.88	13.48	27.03	44.39
16115	6.29	9.51	a	a	a
16116	6.19	10.46	a	a	a
Mean	5.92	9.56	14.55	28.62	45.87
S.D.	0.40	0.71	1.14	1.48	2.60
16211	6.15	11.37	17.94	35.59	52.68
16212	6.29	11.05	a	a	a
16213	7.08	11.04	a	a	a
16214	5.79	9.91	15.30	33.97	51.39
16215	6.61	11.40	18.08	35.94	53.44
16216	6.71	11.77	18.26	34.95	50.46
16201	6.26	10.78	a	a	a
Mean	6.41	11.05	17.40	35.11	51.99
S.D.	0.42	0.59	1.40	0.86	1.33
16311	6.17	7.66	12.80	27.70	42.68
16312	6.56	10.34	a	a	a
16313	6.11	9.30	14.48	30.28	48.99
16314	5.71	9.63	15.81	31.77	49.59
16315	6.00	9.64	a	a	a
16316	6.23	9.89	15.34	30.28	48.25
16317	5.53	8.83	a	a	a
16318	5.99	9.88	a	a	a
Mean	6.04	9.40	14.61	30.01	47.38
S.D.	0.32	0.83	1.32	1.69	3.18
16411	5.83	b	b	b	b
16412	5.61	8.44	12.96	30.05	45.11
16413	5.89	9.10	13.92	30.82	47.58
Mean	5.78	8.77	13.44	30.44	46.35
S.D.	0.15	0.47	0.68	0.54	1.75
16511	5.88	9.68	14.86	31.89	51.80
16512	5.82	9.76	15.20	33.10	54.20
16513	5.83	9.05	14.34	31.40	51.26
16514	5.77	8.02	12.86	29.49	47.74
Mean	5.83	9.13	14.32	31.47	51.25
S.D.	0.05	0.80	1.03	1.50	2.67

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
16611	5.24	8.72	a	a	a
16612	5.21	8.67	a	a	a
16613	5.56	9.05	14.71	31.56	49.90
16614	5.16	8.77	14.17	29.81	47.72
16615	4.94	8.21	13.60	28.89	48.78
16616	5.47	9.13	a	a	a
16617	5.30	8.82	14.17	30.45	47.50
Mean	5.27	8.77	14.16	30.18	48.48
S.D.	0.20	0.30	0.45	1.12	1.10
16711	5.11	8.96	14.36	31.16	46.18
16712	5.45	9.03	13.65	29.82	43.75
16713	5.58	9.29	13.23	31.13	47.17
16714	5.39	9.16	14.33	30.47	45.92
Mean	5.38	9.11	13.89	30.65	45.76
S.D.	0.20	0.15	0.55	0.64	1.44
16811	5.79	8.82	14.66	31.89	48.28
16812	6.05	9.38	15.58	33.12	50.41
16813	5.81	8.74	15.11	33.20	52.02
16814	6.07	9.58	15.62	33.49	51.77
Mean	5.93	9.13	15.24	32.93	50.62
S.D.	0.15	0.41	0.45	0.71	1.71
16911	5.61	9.94	15.60	30.93	47.79
16912	5.87	9.84	14.21	31.10	46.94
16913	5.66	9.70	14.56	28.89	46.65
16914	5.38	9.87	14.99	30.63	47.52
Mean	5.63	9.84	14.84	30.39	47.23
S.D.	0.20	0.10	0.60	1.02	0.52
17011	6.14	8.98	a	a	a
17012	5.72	9.10	a	a	a
17013	5.43	7.32	a	a	a
17014	5.46	7.69	13.17	32.23	50.93
17015	5.42	8.48	13.78	33.14	52.85
17016	6.00	9.50	15.68	35.84	55.99
17017	5.44	b	b	b	b
17018	5.66	8.65	14.72	32.63	53.36
Mean	5.66	8.53	14.34	33.46	53.28
S.D.	0.28	0.78	1.10	1.63	2.09

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
6 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
17111	6.01	9.83	15.60	30.56	48.88
17112	6.31	10.52	16.32	32.35	50.12
17113	6.14	9.51	a	a	a
17114	6.07	9.37	14.53	29.99	48.32
17115	5.86	9.66	15.26	31.51	50.45
Mean	6.08	9.78	15.43	31.10	49.44
S.D.	0.17	0.45	0.74	1.04	1.01
17211	5.22	7.20	a	a	a
17212	5.64	7.49	11.93	29.15	45.91
17213	5.35	7.76	a	a	a
17214	5.59	7.51	11.50	28.85	43.43
17215	5.75	7.88	12.12	28.50	44.47
17216	5.68	8.03	13.08	30.56	47.11
Mean	5.54	7.65	12.16	29.27	45.23
S.D.	0.21	0.30	0.67	0.90	1.61
17311	7.47	9.94	17.72	36.96	57.17
17312	6.85	11.24	18.88	36.98	56.35
Mean	7.16	10.59	18.30	36.97	56.76
S.D.	0.44	0.92	0.82	0.01	0.58
17411	6.49	10.46	17.31	36.11	55.76
17412	6.47	10.88	17.60	37.35	57.57
17413	6.44	11.33	18.36	39.38	65.32
17414	6.65	11.05	17.66	35.79	56.71
17415	6.73	10.74	a	a	a
17416	6.44	10.06	a	a	a
Mean	6.54	10.75	17.73	37.16	58.84
S.D.	0.12	0.45	0.45	1.63	4.38
17511	6.36	8.18	13.40	29.16	45.42
17512	6.10	8.60	a	a	a
17513	6.35	9.15	14.49	29.93	45.80
17514	6.30	8.80	a	a	a
17515	6.58	9.22	14.66	30.23	46.28
17516	5.59	7.60	11.71	26.26	40.94
17517	6.28	9.06	a	a	a
17518	5.92	8.44	a	a	a
Mean	6.19	8.63	13.57	28.90	44.61
S.D.	0.31	0.55	1.36	1.81	2.47

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
17611	6.20	11.09	17.18	31.66	49.55
17612	5.85	10.80	16.90	31.97	51.41
17614	6.11	10.98	17.08	32.67	49.83
17615	6.21	b	b	b	b
17616	5.72	10.58	16.30	31.78	48.86
Mean	6.02	10.86	16.87	32.02	49.91
S.D.	0.22	0.22	0.39	0.45	1.08
17711	5.78	9.17	a	a	a
17712	5.83	9.77	14.65	27.75	48.71
17713	5.63	9.06	13.86	26.51	47.09
17714	6.05	9.47	a	a	a
17715	5.45	8.23	12.69	25.27	43.95
17716	5.56	8.98	a	a	a
17717	5.68	8.87	a	a	a
17718	5.50	8.76	13.26	26.52	46.34
17719	6.27	9.88	a	a	a
Mean	5.75	9.13	13.62	26.51	46.52
S.D.	0.27	0.52	0.84	1.01	1.98
17811	6.55	9.67	14.15	24.03	44.06
17812	6.66	9.49	a	a	a
17813	7.07	9.82	a	a	a
17814	6.41	9.25	a	a	a
17815	6.23	8.95	13.31	25.00	45.25
17816	6.53	9.70	14.31	26.59	44.51
17817	6.95	9.95	a	a	a
17818	6.43	9.33	14.97	26.58	42.14
Mean	6.60	9.52	14.19	25.55	43.99
S.D.	0.28	0.33	0.68	1.26	1.33
17911	6.03	9.74	15.43	31.52	49.40
17912	6.04	9.85	14.97	31.95	52.81
17913	6.21	10.48	16.02	32.58	54.44
Mean	6.09	10.02	15.47	32.02	52.22
S.D.	0.10	0.40	0.53	0.53	2.57

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
18011	5.51	8.48	a	a	a
18012	5.77	8.70	13.38	26.04	43.37
18013	5.99	9.36	14.04	26.78	48.57
18014	5.45	8.62	12.96	25.23	42.97
18015	5.04	7.98	a	a	a
18016	6.16	9.30	14.33	26.58	46.87
Mean	5.65	8.74	13.68	26.16	45.45
S.D.	0.41	0.52	0.62	0.69	2.72
18111	6.36	9.89	a	a	a
18112	5.70	8.34	11.61	20.09	35.32
18113	6.18	9.53	a	a	a
18114	6.54	9.90	14.37	28.67	40.04
18115	5.61	8.78	13.26	26.49	44.19
18116	6.47	10.03	15.19	28.58	45.55
18117	5.54	8.29	a	a	a
Mean	6.06	9.25	13.61	25.96	41.28
S.D.	0.43	0.76	1.55	4.04	4.61
18211	6.51	9.65	a	a	a
18212	5.86	9.27	a	a	a
18213	5.30	8.26	11.72	23.38	40.85
18214	5.89	8.43	12.75	26.24	45.24
18215	5.61	8.98	a	a	a
18216	6.39	9.97	13.79	27.71	45.50
18217	5.93	9.68	a	a	a
18218	5.97	9.14	13.32	27.12	44.92
18219	6.10	9.36	a	a	a
Mean	5.95	9.19	12.90	26.11	44.13
S.D.	0.37	0.57	0.89	1.92	2.20
18311	5.76	9.28	a	a	a
18312	6.02	9.58	15.99	32.70	52.36
18313	6.88	10.33	a	a	a
18314	4.72	8.10	a	a	a
18315	6.10	9.58	16.10	33.33	53.26
18316	5.83	9.33	15.26	32.50	53.39
18317	6.18	9.48	15.80	32.81	51.59
18318	6.28	10.00	a	a	a
18319	5.89	9.19	a	a	a
Mean	5.96	9.43	15.79	32.84	52.65
S.D.	0.57	0.62	0.37	0.35	0.84

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
18411	6.05	9.62	14.79	27.68	43.76
18412	5.53	8.67	13.61	27.71	44.33
18413	6.13	9.72	a	a	a
18414	5.64	8.73	11.90	24.27	41.14
18415	5.87	9.55	a	a	a
18416	6.25	10.23	15.15	29.82	49.54
Mean	5.91	9.42	13.86	27.37	44.69
S.D.	0.28	0.61	1.46	2.30	3.52
18511	6.70	10.51	15.48	28.47	47.88
18512	6.01	9.57	13.85	25.83	41.70
18513	6.44	10.26	a	a	a
18515	6.18	9.74	14.42	27.91	47.82
18516	6.07	9.67	13.65	26.76	46.27
18517	6.60	9.57	a	a	a
Mean	6.33	9.89	14.35	27.24	45.92
S.D.	0.29	0.40	0.82	1.18	2.91
18611	5.93	9.23	13.91	26.89	41.14
18612	5.43	8.25	a	a	a
18613	5.89	9.39	14.49	27.89	41.89
18614	5.15	8.25	13.07	24.65	36.73
18615	6.09	9.17	14.33	27.38	43.27
18616	5.69	8.35	a	a	a
Mean	5.70	8.77	13.95	26.70	40.76
S.D.	0.35	0.54	0.64	1.43	2.83
18711	6.09	9.81	a	a	a
18712	6.48	10.47	16.11	30.40	47.75
18713	6.32	9.86	15.11	28.61	46.42
18714	6.47	10.06	15.11	28.99	49.22
18715	6.63	10.44	15.70	29.70	48.56
Mean	6.40	10.13	15.51	29.43	47.99
S.D.	0.20	0.31	0.49	0.79	1.21
18811	6.15	9.15	14.35	30.60	49.87
18812	5.20	7.91	12.80	27.52	44.79
18813	6.59	10.03	16.15	31.60	47.80
18814	6.40	9.41	a	a	a
18815	5.58	8.52	13.29	28.22	43.89
Mean	5.98	9.00	14.15	29.49	46.59
S.D.	0.58	0.82	1.48	1.93	2.75

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
18911	5.00	7.10	10.79	23.14	35.34
18912	4.66	5.84	9.08	20.64	28.51
Mean	4.83	6.47	9.94	21.89	31.93
S.D.	0.24	0.89	1.21	1.77	4.83
19011	6.09	7.87	a	a	a
19012	5.74	6.88	10.47	22.71	38.19
19013	6.01	7.76	a	a	a
19014	5.74	7.64	a	a	a
19015	5.99	7.84	a	a	a
19016	5.82	b	b	b	b
19017	5.16	6.74	a	a	a
19018	5.43	6.88	10.78	24.03	40.15
19019	5.50	7.02	11.15	23.19	39.62
19020	6.24	8.50	13.12	26.66	44.01
Mean	5.77	7.46	11.38	24.15	40.49
S.D.	0.33	0.60	1.19	1.76	2.49
19111	6.16	9.61	15.30	29.73	47.54
19112	6.00	10.17	16.24	31.74	51.50
19113	5.67	8.85	14.33	28.37	47.21
19114	5.79	9.68	15.46	30.40	50.35
Mean	5.91	9.58	15.33	30.06	49.15
S.D.	0.22	0.55	0.78	1.40	2.11
19211	5.75	8.05	a	a	a
19212	5.27	7.96	11.10	24.22	40.68
19213	5.25	8.10	11.56	22.42	37.37
19214	5.17	7.77	11.14	22.87	37.12
19215	4.98	7.62	10.86	22.33	38.25
Mean	5.28	7.90	11.17	22.96	38.36
S.D.	0.28	0.20	0.29	0.87	1.62

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
19311	5.35	8.20	13.34	30.25	45.49
19312	5.47	8.16	a	a	a
19313	5.27	7.76	a	a	a
19314	5.26	7.66	a	a	a
19315	5.24	7.88	13.03	28.05	42.23
19316	5.40	6.58	10.77	24.92	36.98
19317	5.17	7.51	12.12	27.03	41.02
19318	5.19	8.17	a	a	a
19319	5.36	7.71	a	a	a
19320	5.32	8.31	a	a	a
19305	5.52	8.04	a	a	a
Mean	5.32	7.82	12.32	27.56	41.43
S.D.	0.11	0.48	1.15	2.22	3.52
19411	5.71	8.38	a	a	a
19412	5.97	8.61	a	a	a
19413	6.00	8.72	14.22	30.47	48.56
19414	6.35	8.90	a	a	a
19415	6.02	8.90	14.83	31.86	51.02
19416	6.30	9.12	14.11	30.95	52.38
19417	5.55	8.78	14.52	30.00	50.35
19418	6.31	9.41	a	a	a
19405	6.38	9.69	a	a	a
Mean	6.07	8.95	14.42	30.82	50.58
S.D.	0.30	0.41	0.32	0.79	1.59
19511	5.66	8.41	13.71	28.79	44.06
19512	5.82	8.66	13.67	28.83	43.98
19513	5.69	8.28	14.15	29.07	43.91
19514	5.57	8.21	12.93	27.66	41.96
19515	5.58	8.15	a	a	a
Mean	5.66	8.34	13.62	28.59	43.48
S.D.	0.10	0.20	0.51	0.63	1.01
19611	5.86	9.01	13.13	24.33	41.17
19612	5.49	8.53	a	a	a
19613	5.65	8.52	13.38	24.41	40.73
19614	5.35	7.93	a	a	a
19615	5.80	8.18	12.27	22.97	38.29
19616	5.05	7.55	a	a	a
19617	5.92	9.24	13.66	25.03	42.62
Mean	5.59	8.42	13.11	24.19	40.70
S.D.	0.31	0.59	0.60	0.87	1.80

a = Pup culled on day 4
b = Pup missing on day 4

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

Preweaning Period: Individual Pup Body Weights (Female)
18 mg base/kg/day

DRAFT

Pup #	Day 0	Day 4	Day 7	Day 14	Day 21
19711	5.00	6.43	a	a	a
19712	5.60	7.64	11.95	24.21	38.90
19713	5.75	7.82	a	a	a
19714	5.66	7.29	11.19	23.45	38.26
19715	5.73	8.11	12.01	24.23	39.23
19716	6.02	8.27	12.23	23.87	38.65
19717	5.61	7.99	a	a	a
Mean	5.62	7.65	11.85	23.94	38.76
S.D.	0.31	0.63	0.45	0.37	0.41
19811	6.82	9.97	15.66	27.56	44.69
19812	6.41	9.61	15.28	27.41	46.66
19813	6.64	9.80	15.13	26.68	43.60
19814	6.33	9.72	15.73	27.91	46.32
Mean	6.55	9.78	15.45	27.39	45.32
S.D.	0.22	0.15	0.29	0.52	1.43
19911	4.94	7.10	10.65	23.33	37.20
19912	5.02	7.04	11.08	24.32	38.00
19914	5.28	7.34	11.68	24.68	39.60
19915	4.94	6.93	10.44	22.69	34.92
19916	5.33	7.21	a	a	a
Mean	5.10	7.12	10.96	23.76	37.43
S.D.	0.19	0.16	0.55	0.91	1.95
20011	6.12	9.23	14.79	30.40	50.29
20012	5.93	9.46	15.24	30.98	52.07
20013	6.61	10.26	15.62	30.71	51.75
Mean	6.22	9.65	15.22	30.70	51.37
S.D.	0.35	0.54	0.42	0.29	0.95

a = Pup culled on day 4
b = Pup missing on day 4

POSTWEANING PERIOD: INDIVIDUAL ANIMAL BODY WEIGHTS AND BODY WEIGHT GAIN

Note: During the postweaning period, the individual animal was the experimental unit.

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1011	95	153	217	289	357	399	445	b	b	b	b	b
1013	100	154	210	273	327	370	404	427	457	475	498	513
1021	102	160	216	274	329	372	411	b	b	b	b	b
1024	98	150	211	273	328	381	413	431	464	485	504	524
1032	103	160	214	278	337	387	421	b	b	b	b	b
1036	111	174	231	301	369	417	452	489	529	567	593	618
1043	102	158	212	269	318	361	393	b	b	b	b	b
1047	98	153	209	275	331	372	408	432	462	482	494	509
1052	108	172	233	294	350	384	410	b	b	b	b	b
1054	98	150	209	271	331	371	398	429	460	480	503	516
1065	95	147	195	252	302	345	383	b	b	b	b	b
1066	102	164	218	278	345	391	430	461	495	529	543	549
1071	94	149	202	263	330	371	410	b	b	b	b	b
1072	104	160	221	294	360	408	449	485	529	562	587	607
1083	106	166	235	305	364	410	436	b	b	b	b	b
1084	105	160	222	287	352	406	440	466	498	531	554	561
1091	105	167	232	290	344	387	421	b	b	b	b	b
1097	97	164	223	283	342	388	421	439	472	495	528	552
1102	99	156	222	292	354	401	447	b	b	b	b	b
1104	108	166	233	298	362	405	442	472	497	521	535	553
1112	99	154	215	278	344	388	425	b	b	b	b	b
1113	112	179	244	310	363	414	453	483	508	530	548	576
1125	93	152	211	273	323	372	402	b	b	b	b	b
1127	87	146	205	267	322	373	413	433	476	506	531	548
1135	99	154	210	272	317	361	387	b	b	b	b	b
1136	108	173	238	303	370	418	457	481	516	509	549	572
1146	80	136	199	267	328	375	432	b	b	b	b	b
1148	93	155	220	289	341	394	434	463	489	514	534	553
1152	87	144	202	263	306	347	386	b	b	b	b	b
1153	92	149	190	269	321	378	415	440	476	504	531	541
1161	96	150	209	271	323	372	412	b	b	b	b	b
1162	103	163	225	292	348	396	443	464	501	533	552	572
1173	103	158	216	264	290	341	379	b	b	b	b	b
1174	105	166	227	286	334	375	400	420	443	458	479	489
1185	105	162	232	287	347	396	443	b	b	b	b	b
1189	105	164	229	294	345	395	441	457	480	499	531	550
1192	108	173	241	315	382	433	485	b	b	b	b	b
1193	108	171	233	300	363	416	464	496	533	551	578	602
1202	94	151	210	269	326	376	425	b	b	b	b	b
1203	84	136	199	262	319	352	389	406	439	460	479	488

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1214	98	163	235	296	319	371	422	b	b	b	b	b
1215	99	164	235	312	379	445	501	545	582	614	653	583
1223	96	152	219	286	345	395	436	b	b	b	b	b
1226	87	140	197	252	300	344	375	402	422	438	445	466
1233	91	152	223	297	369	434	490	b	b	b	b	b
1236	92	148	210	269	304	365	410	443	486	511	540	551
1242	87	137	198	259	315	363	415	b	b	b	b	b
1248	92	146	212	278	345	404	449	485	515	544	575	598
1251	100	163	222	292	345	386	438	b	b	b	b	b
12515	103	164	231	300	356	407	445	485	518	542	555	579
MEAN	99	157	218	282	338	386	426	457	490	514	537	551
S.D.	7.3	10.2	13.2	15.7	21.4	23.8	27.8	32.7	35.2	39.0	43.0	38.8
N	50	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1011	b	b
1013	533	541
1021	b	b
1024	539	553
1032	b	b
1036	644	657
1043	b	b
1047	534	536
1052	b	b
1054	537	549
1065	b	b
1066	563	572
1071	b	b
1072	624	629
1083	b	b
1084	580	602
1091	b	b
1097	570	577
1102	b	b
1104	574	586
1112	b	b
1113	589	609
1125	b	b
1127	573	585
1135	b	b
1136	602	623
1146	b	b
1148	--	--
1152	b	b
1153	--	--
1161	b	b
1162	--	--
1173	b	b
1174	--	--
1185	b	b
1189	--	--
1192	b	b
1193	--	--
1202	b	b
1203	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1214	b	b
1215	--	--
1223	b	b
1226	--	--
1233	b	b
1236	--	--
1242	b	b
1248	--	--
1251	b	b
12515	--	--
MEAN	574	586
S.D.	34.7	36.9
N	13	13

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1264	114	187	257	327	394	449	495	b	b	b	b	b
1267	109	177	234	294	354	380	404	427	455	470	496	511
1275	99	132	208	270	325	366	404	b	b	b	b	b
1277	99	138	215	282	348	397	439	461	496	522	540	564
1283	94	157	224	294	353	401	447	b	b	b	b	b
1286	100	157	224	295	366	423	472	511	552	575	592	622
1295	110	158	217	283	340	388	438	b	b	b	b	b
1296	108	165	232	311	381	426	452	487	528	559	586	607
1307	107	168	229	302	367	415	459	b	b	b	b	b
1309	108	167	224	292	353	400	422	445	478	496	512	536
1311	107	173	240	314	372	403	451	b	b	b	b	b
1312	109	168	234	304	365	417	456	482	513	541	569	591
1322	109	174	239	308	376	426	479	b	b	b	b	b
1323	114	181	255	323	382	400	477	502	541	563	599	620
1331	94	148	206	259	317	358	396	b	b	b	b	b
1333	93	146	211	263	315	357	392	419	449	473	497	506
1341	94	149	207	265	313	350	377	b	b	b	b	b
1343	97	163	225	294	353	405	442	473	509	499	549	564
1353	95	153	213	280	340	390	432	b	b	b	b	b
1354	88	135	169	232	290	338	372	403	430	455	471	496
1361	90	150	214	280	341	395	433	b	b	b	b	b
1365	97	162	228	300	358	414	448	483	514	554	568	585
1375	92	142	198	252	299	339	371	b	b	b	b	b
1379	99	153	214	272	331	380	406	440	469	486	508	519
1382	100	165	226	288	345	393	428	b	b	b	b	b
1383	100	162	228	294	342	391	420	455	487	516	534	548
1392	94	154	212	266	323	362	400	b	b	b	b	b
1394	98	161	222	285	345	390	428	458	494	518	544	564
1401	89	143	206	274	339	393	436	b	b	b	b	b
1404	87	133	184	251	301	348	387	403	431	461	485	511
1414	98	154	223	292	354	409	449	b	b	b	b	b
1415	102	160	225	284	342	383	421	431	473	498	525	545
1421	91	147	203	273	327	378	417	b	b	b	b	b
1428	95	150	215	296	361	431	491	526	559	595	620	657
1432	104	166	233	306	370	430	478	b	b	b	b	b
1434	97	162	228	302	292	245	372	452	493	529	561	594
1443	89	145	208	277	340	384	424	b	b	b	b	b
1444	90	149	205	261	310	356	390	415	445	464	477	501
1452	84	143	215	282	348	404	449	b	b	b	b	b
1454	78	137	203	267	335	388	424	447	488	514	548	571

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1461	99	161	227	292	358	405	456	b	b	b	b	b
1463	96	149	223	282	322	368	415	447	479	508	534	555
1474	88	116	191	255	321	374	413	b	b	b	b	b
1475	87	148	214	280	343	397	389	436	487	522	548	584
1483	98	159	230	294	360	405	441	b	b	b	b	b
1484	94	153	221	293	357	407	448	481	506	526	417	517
1491	84	145	221	303	384	465	532	b	b	b	b	b
1493	101	161	226	293	345	372	407	425	447	464	480	496
1501	95	149	213	274	329	376	409	b	b	b	b	b
1503	98	155	219	272	329	378	413	441	472	496	529	537
MEAN	97	155	219	285	343	389	430	454	488	512	532	556
S.D.	8.1	13.3	15.6	19.2	24.1	33.9	34.4	32.6	35.1	37.8	46.4	44.1
N	50	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1264	b	b
1267	517	530
1275	b	b
1277	569	592
1283	b	b
1286	640	660
1295	b	b
1296	622	636
1307	b	b
1309	550	563
1311	b	b
1312	615	624
1322	b	b
1323	647	666
1331	b	b
1333	536	553
1341	b	b
1343	592	606
1353	b	b
1354	510	520
1361	b	b
1365	604	624
1375	b	b
1379	538	550
1382	b	b
1383	557	566
1392	b	b
1394	--	--
1401	b	b
1404	--	--
1414	b	b
1415	--	--
1421	b	b
1428	--	--
1432	b	b
1434	--	--
1443	b	b
1444	--	--
1452	b	b
1454	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1461	b	b
1463	--	--
1474	b	b
1475	--	--
1483	b	b
1484	--	--
1491	b	b
1493	--	--
1501	b	b
1503	--	--
MEAN	577	592
S.D.	46.3	48.4
N	13	13

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1511	109	165	226	295	352	402	438	b	b	b	b	b
1515	112	169	227	298	357	403	428	450	488	503	531	545
1523	105	169	234	305	371	427	474	b	b	b	b	b
1524	100	162	222	292	352	403	441	466	496	518	409	511
1532	93	152	213	279	338	375	411	b	b	b	b	b
1533	90	137	188	257	308	354	391	413	448	472	493	507
1542	98	146	200	261	319	352	393	b	b	b	b	b
1544	94	138	195	257	316	370	418	439	475	497	506	538
1554	106	167	231	311	374	443	497	b	b	b	b	b
1555	95	157	219	291	357	406	452	480	509	547	566	581
1561	93	156	221	292	349	398	445	b	b	b	b	b
1566	99	163	232	309	375	422	459	477	504	528	547	570
1571	106	167	229	303	361	419	461	b	b	b	b	b
1574	100	165	219	290	345	393	427	454	479	504	528	535
1584	91	150	213	288	348	395	435	b	b	b	b	b
1585	88	143	204	274	334	375	408	422	445	472	494	513
1603	89	141	205	260	323	366	409	b	b	b	b	b
1605	99	158	221	279	343	387	431	456	489	515	534	556
1611	89	142	192	251	302	353	388	b	b	b	b	b
1612	78	129	183	238	287	327	357	379	406	426	442	461
1622	94	149	211	280	334	388	426	b	b	b	b	b
1625	103	166	228	294	352	401	441	469	502	529	551	572
1634	96	152	214	282	337	386	442	b	b	b	b	b
1636	91	147	214	271	325	370	410	436	474	492	515	536
1644	89	142	197	262	319	323	378	b	b	b	b	b
1646	82	130	181	246	292	339	380	404	436	464	497	525
1652	97	157	224	291	340	389	433	b	b	b	b	b
1658	99	161	219	286	338	385	419	454	480	503	528	548
1661	93	143	202	265	321	365	408	b	b	b	b	b
1664	91	146	206	272	322	367	398	429	458	485	511	538
1672	90	149	209	284	342	391	432	b	b	b	b	b
1673	98	161	224	305	365	419	466	512	543	584	606	634
1681	99	162	230	313	375	432	480	b	b	b	b	b
1685	94	152	220	291	357	423	472	502	550	577	603	627
1691	88	143	199	258	297	335	340	b	b	b	b	b
1692	89	147	207	279	326	372	413	431	460	479	501	524
1704	96	152	216	282	331	375	408	b	b	b	b	b
1706	92	148	213	270	320	357	390	413	438	456	486	503
1714	96	152	211	276	334	378	419	b	b	b	b	b
1715	105	170	234	301	365	411	449	475	494	521	537	550

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

Note: There was no litter F_1 litter No. 159 since F_0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1723	80	130	186	243	287	331	377	b	b	b	b	b
1727	84	130	192	253	319	376	419	443	489	512	520	545
1733	111	169	235	303	366	419	473	b	b	b	b	b
1734	109	179	254	324	387	448	498	528	557	583	599	625
1741	109	177	248	321	377	429	483	b	b	b	b	b
1743	107	174	241	309	366	415	460	485	525	560	580	611
1754	89	144	204	266	323	367	406	b	b	b	b	b
1755	83	142	202	267	314	363	410	447	487	510	539	566
MEAN	96	153	214	282	338	386	427	453	485	510	526	551
S.D.	8.3	12.9	16.7	21.1	25.1	30.8	35.2	35.2	36.9	40.2	46.8	42.4
N	48	48	48	48	48	48	48	24	24	24	24	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1511	b	b
1515	574	581
1523	b	b
1524	543	563
1532	b	b
1533	526	537
1542	b	b
1544	559	572
1554	b	b
1555	608	625
1561	b	b
1566	584	598
1571	b	b
1574	556	568
1584	b	b
1585	521	532
1603	b	b
1605	581	597
1611	b	b
1612	479	493
1622	b	b
1625	593	614
1634	b	b
1636	--	--
1644	b	b
1646	--	--
1652	b	b
1658	--	--
1661	b	b
1664	--	--
1672	b	b
1673	--	--
1681	b	b
1685	--	--
1691	b	b
1692	--	b
1704	b	b
1706	--	--
1714	b	b
1715	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

Note: There was no litter F_1 litter No. 159 since F_0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1723	b	b
1727	--	--
1733	b	b
1734	--	--
1741	b	b
1743	--	--
1754	b	b
1755	--	--
MEAN	557	571
S.D.	37.5	38.9
N	11	11

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 28[a]	PNO 35	PND 42	PND 49	PND 56	PND 63	PNO 70	PND 77[c]	PND 84	PNO 91	PNO 98	PND 105
1762	93	152	211	273	326	370	409	b	b	b	b	b
1763	96	157	217	277	337	384	425	456	482	505	533	549
1773	93	154	219	282	337	381	422	b	b	b	b	b
1774	92	149	209	277	333	376	409	425	456	478	502	526
1782	89	146	212	268	328	366	398	b	b	b	b	b
1783	86	141	204	268	326	375	417	442	472	491	506	520
1792	96	151	207	277	340	396	425	b	b	b	b	b
1795	95	151	204	260	315	355	386	408	434	453	477	494
1801	83	138	193	250	316	369	416	b	b	b	b	b
1806	83	140	197	263	245	330	382	422	456	487	516	538
1813	94	148	204	264	326	366	402	b	b	b	b	b
1814	93	148	206	270	328	373	418	445	474	498	514	531
1823	88	143	201	239	252	321	371	b	b	b	b	b
1824	88	141	196	265	324	371	422	449	481	510	532	560
1831	98	158	225	294	354	393	429	b	b	b	b	b
1835	96	151	216	282	339	385	426	458	495	525	549	568
1845	87	141	201	265	325	373	407	b	b	b	b	b
1846	84	131	192	250	310	361	408	442	483	510	534	554
1852	90	146	207	267	328	383	421	b	b	b	b	b
1853	97	160	229	301	372	426	475	507	552	581	605	627
1861	81	140	196	257	309	357	374	b	b	b	b	b
1865	73	122	167	213	257	290	311	332	360	382	397	406
1873	88	140	191	255	313	360	388	b	b	b	b	b
1875	83	136	197	256	300	341	373	401	426	455	474	495
1882	100	160	225	297	362	420	478	b	b	b	b	b
1883	94	154	214	273	334	377	418	442	472	498	511	532
1894	88	148	216	294	352	412	456	b	b	b	b	b
1897	80	132	187	249	299	341	369	374	414	443	468	491
1901	84	142	204	259	318	364	403	b	b	b	b	b
1904	82	139	197	254	309	355	391	418	446	470	494	512
1912	98	152	206	277	337	393	409	b	b	b	b	b
1914	93	147	214	291	349	410	460	472	506	542	586	610
1921	82	138	190	258	313	373	414	b	b	b	b	b
1924	76	127	183	248	315	370	422	447	487	523	546	571
1934	80	133	193	257	314	372	420	b	b	b	b	b
1936	80	133	189	252	304	359	402	424	462	494	516	539
1941	89	143	200	266	328	371	412	b	b	b	b	b
1942	102	174	242	314	382	434	472	508	546	579	611	637
1952	82	133	193	254	314	371	412	b	b	b	b	b
1956	91	147	212	272	333	380	416	443	474	500	521	540

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
1962	89	144	199	253	302	337	368	b	b	b	b	b
1965	82	138	198	256	311	363	392	416	442	461	479	492
1972	87	140	203	263	323	370	404	b	b	b	b	b
1974	76	124	183	233	285	335	378	399	429	465	489	507
1982	88	144	202	264	321	366	406	b	b	b	b	b
1988	94	152	216	280	335	382	416	444	466	493	516	525
1991	69	118	178	246	308	373	425	b	b	b	b	b
1993	76	126	187	251	311	369	410	435	475	501	527	548
2005	95	153	214	269	329	371	406	b	b	b	b	b
2008	95	155	215	276	329	374	411	426	449	475	494	512
MEAN	88	144	203	266	321	371	410	433	466	493	516	535
S.D.	7.4	10.8	13.8	18.0	25.5	25.3	28.9	36.6	39.3	41.4	44.7	47.5
N	50	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1762	b	b
1763	570	585
1773	b	b
1774	543	558
1782	b	b
1783	534	543
1792	b	b
1795	514	521
1801	b	b
1806	565	577
1813	b	b
1814	549	559
1823	b	b
1824	581	598
1831	b	b
1835	593	601
1845	b	b
1846	573	597
1852	b	b
1853	657	684
1861	b	b
1865	430	402
1873	b	b
1875	514	531
1882	b	b
1883	--	--
1894	b	b
1897	--	--
1901	b	b
1904	--	--
1912	b	b
1914	--	--
1921	b	b
1924	--	--
1934	b	b
1936	--	--
1941	b	b
1942	--	--
1952	b	b
1956	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1962	b	b
1965	--	--
1972	b	b
1974	--	--
1982	b	b
1988	--	--
1991	b	b
1993	--	--
2005	b	b
2008	--	--
MEAN	552	563
S.D.	54.5	66.3
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
10112	92	117	162	190	214	225	243	b	b	b	b	b
10113	96	125	175	208	236	259	275	316	361	421	338	376
10214	89	133	176	193	213	242	249	b	b	b	b	b
10217	95	137	179	204	235	247	277	294	340	413	350	340
10315	90	129	152	180	204	218	233	b	b	b	b	b
10318	95	136	165	177	214	243	262	288	327	386	318	330
10412	97	134	171	203	186	225	246	b	b	b	b	b
10413	90	128	156	170	206	220	238	276	317	393	291	281
10511	84	118	146	165	189	198	208	b	b	b	b	b
10513	87	132	160	182	205	221	234	273	307	287	b	b
10614	94	133	171	191	209	229	244	b	b	b	b	b
10616	97	132	160	180	197	211	229	255	295	371	284	301
10712	96	136	170	199	224	239	254	b	b	b	b	b
10713	89	128	165	191	213	247	280	319	361	429	365	396
10813	97	140	165	188	210	226	237	b	b	b	b	b
10815	93	134	160	176	204	223	233	265	297	364	291	291
10911	92	134	172	195	214	223	249	279	317	393	309	320
11012	89	132	176	197	231	254	281	b	b	b	b	b
11015	97	141	184	214	245	268	296	337	386	477	372	364
11111	96	135	176	203	220	231	252	b	b	b	b	b
11117	89	131	162	189	208	230	244	275	310	390	298	308
11212	83	126	153	175	189	203	222	b	b	b	b	b
11213	94	136	171	198	219	241	260	288	325	420	316	319
11315	90	123	166	167	210	241	252	b	b	b	b	b
11316	97	146	183	220	243	261	278	309	346	430	342	367
11412	85	128	161	192	206	232	249	b	b	b	b	b
11414	92	139	166	203	228	256	278	313	356	425	340	373
11511	85	124	157	183	200	212	214	b	b	b	b	b
11519	78	124	156	178	197	219	237	272	306	390	296	308
11611	97	143	172	203	213	232	247	b	b	b	b	b
11612	93	136	166	195	219	251	264	302	334	409	318	315
11711	92	126	161	174	196	206	227	b	b	b	b	b
11712	85	121	151	170	185	200	211	251	286	356	243	261
11812	96	144	180	203	211	218	252	b	b	b	b	b
11814	92	132	158	176	197	213	224	256	296	368	301	298
11911	97	148	193	225	246	266	284	b	b	b	b	b
11915	108	157	195	218	247	261	278	304	315	330	b	b
12012	81	128	157	180	206	226	240	b	b	b	b	b
12013	85	127	168	197	203	238	259	288	322	370	320	360
12113	92	134	169	196	218	242	270	b	b	b	b	b

[a]Two animals/sex/litter were evaluated from PND28 - 70. There was only one female in litter No. 109.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
12114	96	142	180	213	233	252	270	318	348	417	346	340
12211	79	112	141	163	179	198	214	b	b	b	b	b
12213	89	130	163	192	211	228	247	274	306	399	284	278
12312	84	124	148	179	197	209	227	b	b	b	b	b
12313	83	121	151	173	189	206	220	253	290	373	270	274
12411	76	118	152	186	193	201	225	b	b	b	b	b
12413	73	113	151	182	208	230	252	284	307	303	b	b
12511	91	140	162	199	222	241	265	b	b	b	b	b
12519	94	144	180	202	232	255	268	307	339	386	347	335
MEAN	90	132	166	191	212	231	249	288	324	388	315	324
S.D.	6.6	9.2	11.8	14.9	16.8	19.2	21.7	23.5	25.7	41.1	32.4	37.2
N	49	49	49	49	49	49	49	25	25	25	22	22

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
10112	b	b
10113	382	376
10214	b	b
10217	345	333
10315	b	b
10318	346	372
10412	b	b
10413	293	298
10511	b	b
10513	b	b
10614	b	b
10616	311	304
10712	b	b
10713	396	395
10813	b	b
10815	290	305
10911	327	323
11012	b	b
11015	380	387
11111	b	b
11117	319	318
11212	b	b
11213	323	328
11315	b	b
11316	366	380
11412	b	b
11414	--	--
11511	b	b
11519	--	--
11611	b	b
11612	--	--
11711	b	b
11712	--	--
11812	b	b
11814	--	--
11911	b	b
11915	b	b
12012	b	b
12013	--	--
12113	b	b

--:Data unavailable.
[b]Scheduled sacrifice.

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
12114	--	--
12211	b	b
12213	--	--
12312	b	b
12313	--	--
12411	b	b
12413	b	b
12511	b	b
12519	--	--
MEAN	340	343
S.D.	35.3	36.0
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
12611	101	145	173	207	234	255	266	b	b	b	b	b
12612	99	146	184	210	248	266	287	323	359	447	324	343
12715	85	127	160	183	205	231	241	b	b	b	b	b
12716	87	129	162	191	219	245	257	300	343	437	313	327
12813	96	138	181	206	239	259	284	b	b	b	b	b
12815	91	132	169	199	243	261	287	313	348	397	344	380
12911	99	139	172	203	228	252	271	b	b	b	b	b
12912	100	138	167	201	227	243	265	289	310	302	306	b
13011	96	140	174	199	223	235	253	b	b	b	b	b
13013	103	158	202	235	272	302	210	316	374	440	374	385
13113	98	142	179	201	220	243	261	b	b	b	b	b
13114	97	145	183	206	233	248	267	302	338	416	312	340
13212	98	147	175	215	238	254	279	b	b	b	b	b
13213	104	150	178	208	233	247	261	302	347	398	338	341
13315	92	135	168	192	215	241	256	b	b	b	b	b
13317	95	135	170	197	229	252	274	312	351	434	318	339
13412	85	124	153	183	203	225	244	b	b	b	b	b
13414	86	132	166	193	223	248	268	300	326	403	321	328
13512	87	124	150	172	202	220	240	b	b	b	b	b
13515	84	124	155	181	208	215	233	259	288	398	272	290
13612	97	142	179	199	233	254	276	b	b	b	b	b
13614	98	143	184	218	243	259	274	316	353	441	338	348
13711	86	118	150	169	197	219	230	b	b	b	b	b
13713	94	138	168	202	228	244	259	298	328	377	335	337
13811	85	127	169	189	224	246	279	b	b	b	b	b
13815	99	149	182	202	235	258	277	315	359	438	344	351
13912	95	142	175	179	227	243	259	b	b	b	b	b
13913	90	126	166	189	209	221	245	293	325	413	308	302
14011	84	126	154	185	202	224	235	b	b	b	b	b
14014	82	123	153	188	200	224	238	268	306	399	302	305
14111	91	133	175	201	224	256	281	b	b	b	b	b
14112	88	129	164	203	226	249	260	288	325	370	327	324
14212	82	124	153	189	201	217	232	b	b	b	b	b
14213	86	134	166	194	222	243	264	291	320	368	326	336
14314	85	134	171	205	226	254	279	b	b	b	b	b
14315	84	124	157	187	209	223	248	287	328	383	316	362
14412	89	128	164	192	209	230	244	275	303	373	284	290
14416	85	129	161	185	213	235	181	b	b	b	b	b
14511	75	121	160	190	210	234	248	b	b	b	b	b
14514	73	124	164	184	214	237	262	290	322	383	319	323

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
14613	89	135	171	206	229	248	249	b	b	b	b	b
14615	89	133	158	194	231	246	257	295	340	404	324	326
14712	85	132	161	188	212	230	244	b	b	b	b	b
14714	84	132	172	201	233	259	286	310	353	414	346	349
14811	86	133	170	183	213	227	239	b	b	b	b	b
14812	85	128	173	198	216	244	267	299	342	405	344	352
14913	96	145	178	204	231	250	274	b	b	b	b	b
14916	83	131	158	190	221	242	271	323	377	473	344	377
15011	84	124	159	190	207	225	238	b	b	b	b	b
15013	87	129	158	184	201	210	236	262	292	357	286	294
MEAN	90	134	168	195	222	242	257	297	334	403	323	335
S.D.	7.1	8.8	10.6	11.9	14.8	16.4	20.9	17.6	23.4	35.6	22.6	26.6
N	50	50	50	50	50	50	50	25	25	25	25	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
12611	b	b
12612	356	373
12715	b	b
12716	349	358
12813	b	b
12815	381	394
12911	b	b
12912	b	b
13011	b	b
13013	402	396
13113	b	b
13114	342	343
13212	b	b
13213	348	362
13315	b	b
13317	359	369
13412	b	b
13414	348	361
13512	b	b
13515	294	292
13612	b	b
13614	351	365
13711	b	b
13713	344	354
13811	b	b
13815	359	374
13912	b	b
13913	--	--
14011	b	b
14014	--	--
14111	b	b
14112	--	--
14212	b	b
14213	--	--
14314	b	b
14315	--	--
14412	--	--
14416	b	b
14511	b	b
14514	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
14613	b	b
14615	--	--
14712	b	b
14714	--	--
14811	b	b
14812	--	--
14913	b	b
14916	--	--
15011	b	b
15013	--	--
MEAN	353	362
S.D.	25.3	26.7
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
15112	93	127	162	187	208	236	254	b	b	b	b	b
15115	105	151	188	216	250	272	292	325	363	424	359	355
15211	90	127	163	180	205	217	229	b	b	b	b	b
15213	94	140	172	200	223	239	258	287	316	378	330	350
15313	91	133	168	185	212	221	250	b	b	b	b	b
15314	85	124	160	183	212	231	245	280	313	370	317	338
15412	86	126	164	194	216	239	264	b	b	b	b	b
15416	94	136	167	194	219	244	263	283	318	401	329	348
15513	92	135	176	207	241	266	291	b	b	b	b	b
15518	95	144	181	204	148	229	246	273	313	372	321	349
15611	98	146	187	225	256	277	306	b	b	b	b	b
15617	94	141	177	204	247	266	298	328	363	445	360	396
15712	89	127	156	190	210	228	237	b	b	b	b	b
15714	96	142	174	202	217	244	263	309	352	443	341	343
15814	85	124	162	191	220	241	274	b	b	b	b	b
15816	83	130	167	188	224	248	273	279	312	363	466	338
16011	86	125	159	183	205	224	245	b	b	b	b	b
16015	89	126	159	181	202	216	231	265	291	355	294	298
16113	76	114	147	170	186	213	232	b	b	b	b	b
16114	79	122	159	179	193	215	228	267	299	374	290	289
16211	87	110	158	180	196	213	235	b	b	b	b	b
16216	84	109	149	164	183	200	219	250	288	355	275	301
16311	80	122	155	181	197	218	233	b	b	b	b	b
16313	83	119	158	175	198	214	226	260	312	380	286	301
16412	81	120	151	175	194	209	226	b	b	b	b	b
16413	80	128	161	195	215	236	260	292	327	372	325	336
16513	88	132	168	209	235	260	275	b	b	b	b	b
16514	84	131	178	215	241	264	285	314	354	449	343	364
16613	87	131	158	183	197	208	215	b	b	b	b	b
16614	83	127	160	191	208	228	241	273	303	370	280	287
16711	83	129	160	180	204	228	241	b	b	b	b	b
16714	81	125	159	178	197	215	224	268	299	339	393	342
16813	91	133	179	205	236	261	282	b	b	b	b	b
16814	90	133	171	193	150	231	243	289	328	388	323	328
16911	79	121	146	174	184	201	211	b	b	b	b	b
16913	83	125	159	190	213	214	234	261	296	395	273	289
17016	94	139	167	196	213	235	254	b	b	b	b	b
17018	87	131	163	187	213	231	249	274	301	386	286	304
17111	94	138	170	196	214	234	249	b	b	b	b	b
17115	89	131	162	182	213	232	249	278	310	378	319	320

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

Note: There was no litter F_1 litter No. 159 since F_0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
17212	79	125	162	183	206	231	247	b	b	b	b	b
17215	73	114	147	176	203	219	233	254	276	326	270	275
17311	96	150	204	235	261	287	309	b	b	b	b	b
17312	91	134	160	180	201	204	219	256	295	384	286	294
17411	96	144	188	223	255	283	303	b	b	b	b	b
17413	107	153	192	220	196	276	297	349	383	430	368	391
17513	87	130	167	198	218	240	272	b	b	b	b	b
17516	73	113	144	171	191	215	232	267	298	391	271	295
MEAN	88	130	166	192	211	234	253	283	317	386	321	326
S.D.	7.3	10.3	12.6	15.7	23.2	22.5	26.1	25.5	27.3	32.2	46.2	33.2
N	48	48	48	48	48	48	48	24	24	24	24	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
15112	b	b
15115	347	359
15211	b	b
15213	345	341
15313	b	b
15314	338	332
15412	b	b
15416	339	333
15513	b	b
15518	359	367
15611	b	b
15617	396	407
15712	b	b
15714	355	355
15814	b	b
15816	330	355
16011	b	b
16015	299	309
16113	b	b
16114	292	286
16211	b	b
16216	293	286
16311	b	b
16313	--	--
16412	b	b
16413	--	--
16513	b	b
16514	--	--
16613	b	b
16614	--	--
16711	b	b
16714	--	--
16813	b	b
16814	--	--
16911	b	b
16913	--	--
17016	b	b
17018	--	--
17111	b	b
17115	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

Note: There was no litter F_1 litter No. 159 since F_0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
17212	b	b
17215	--	--
17311	b	b
17312	--	--
17411	b	b
17413	--	--
17513	b	b
17516	--	--
MEAN	336	339
S.D.	31.5	36.0
N	11	11

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
17614	86	125	155	184	211	230	237	b	b	b	b	b
17616	81	117	152	174	198	219	231	266	280	270	b	b
17712	92	138	168	194	216	237	254	b	b	b	b	b
17713	83	124	158	181	203	225	240	275	314	376	287	308
17815	83	125	150	168	197	208	218	b	b	b	b	b
17816	80	122	152	177	202	221	237	276	320	353	319	315
17911	83	119	149	167	207	228	236	b	b	b	b	b
17912	95	136	170	191	219	238	257	294	335	402	327	324
18013	83	120	160	182	206	230	253	b	b	b	b	b
18014	76	113	143	170	195	215	235	288	322	407	307	314
18112	66	96	119	142	160	172	181	b	b	b	b	b
18116	81	108	140	156	171	176	188	227	276	359	240	238
18213	69	102	126	151	171	189	206	b	b	b	b	b
18214	75	112	140	168	186	213	232	274	315	397	319	328
18315	92	133	177	206	238	270	293	b	b	b	b	b
18317	89	123	160	186	218	237	253	290	328	427	335	354
18411	71	108	134	158	178	192	207	b	b	b	b	b
18416	88	130	164	193	214	233	256	298	350	440	319	338
18511	89	132	162	190	223	245	265	b	b	b	b	b
18515	86	126	158	173	212	238	259	284	334	405	339	353
18611	74	116	143	162	183	198	206	b	b	b	b	b
18613	74	105	132	154	170	185	201	206	255	336	257	264
18712	85	126	153	175	198	220	231	b	b	b	b	b
18714	81	121	147	176	193	220	238	270	311	386	291	297
18812	82	130	168	192	217	244	258	b	b	b	b	b
18815	87	138	175	206	252	282	306	333	346	367	b	b
18911	75	118	162	200	233	263	274	b	b	b	b	b
18912	61	103	142	180	210	241	260	280	310	341	350	357
19012	70	114	154	174	197	216	235	b	b	b	b	b
19019	73	118	155	177	202	222	234	275	300	374	283	298
19112	96	148	181	214	237	263	279	b	b	b	b	b
19114	90	137	170	203	221	251	273	309	345	427	340	361
19214	71	109	141	174	196	216	224	b	b	b	b	b
19215	71	110	142	170	192	218	231	262	295	352	312	312
19315	86	134	176	208	236	260	291	b	b	b	b	b
19317	76	118	152	184	197	231	254	289	336	421	315	331
19415	88	131	160	186	209	225	246	b	b	b	b	b
19416	93	144	167	197	217	237	253	284	323	391	319	324
19512	79	116	156	190	213	231	259	b	b	b	b	b
19514	74	113	149	173	198	219	232	260	306	381	308	313

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[b]Scheduled sacrifice.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 28[a]	PND 35	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[c]	PND 84	PND 91	PND 98	PND 105
19613	71	116	140	164	176	198	223	b	b	b	b	b
19617	76	116	148	175	204	227	247	277	325	385	317	330
19715	72	112	143	166	182	196	203	b	b	b	b	b
19716	72	115	155	174	199	218	232	267	308	380	290	297
19812	84	126	161	192	221	247	274	283	311	328	b	b
19814	88	135	176	206	228	240	197	b	b	b	b	b
19912	67	104	141	166	196	214	238	b	b	b	b	b
19915	65	101	136	154	179	198	214	245	280	362	257	277
20011	93	134	173	204	235	248	236	b	b	b	b	b
20D12	86	134	185	204	234	245	271	300	333	418	330	334
MEAN	80	121	154	180	205	226	241	276	314	379	307	317
S.D.	8.7	12.0	14.6	16.9	20.4	23.4	27.0	25.3	23.6	37.8	28.8	30.4
N	50	50	50	50	50	50	50	25	25	25	22	22

--: Data Unavailable b: Scheduled Sacrifice

[a]Two animals/sex/litter were evaluated from PND28 - 70.
[c]One animal/sex/litter was evaluated from PND77 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
17614	b	b
17616	b	b
17712	b	b
17713	320	318
17815	b	b
17816	316	323
17911	b	b
17912	332	341
18013	b	b
18014	311	325
18112	b	b
18116	241	235
18213	b	b
18214	341	341
18315	b	b
18317	345	343
18411	b	b
18416	337	343
18511	b	b
18515	362	377
18611	b	b
18613	263	258
18712	b	b
18714	309	313
18812	b	b
18815	b	b
18911	b	b
18912	b	b
19012	b	b
19019	--	--
19112	b	b
19114	--	--
19214	b	b
19215	--	--
19315	b	b
19317	--	--
19415	b	b
19416	--	--
19512	b	b
19514	--	--

--:Data unavailable.
[b]Scheduled sacrifice.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL BODY WEIGHTS (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND-119
19613	b	b
19617	--	--
19715	b	b
19716	--	--
19812	b	b
19814	b	b
19912	b	b
19915	--	--
20011	b	b
20012	--	--
MEAN	316	320
S.D.	35.8	40.4
N	11	11

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1011	58	64	72	68	42	46	b	b	b	b	b
1013	54	56	63	54	43	34	23	30	18	23	15
1021	58	56	58	55	43	39	b	b	b	b	b
1024	52	61	62	55	53	32	18	33	21	19	20
1032	57	54	64	59	50	34	b	b	b	b	b
1036	63	57	70	68	48	35	37	40	38	26	25
1043	56	54	57	49	43	32	b	b	b	b	b
1047	55	56	66	56	41	36	24	30	20	12	15
1052	64	61	61	56	34	26	b	b	b	b	b
1054	52	59	62	60	40	27	31	31	20	23	13
1065	52	48	57	50	43	38	b	b	b	b	b
1066	62	54	60	67	46	39	31	34	34	14	6
1071	55	53	61	67	41	39	b	b	b	b	b
1072	56	61	73	66	48	41	36	44	33	25	20
1083	60	69	70	59	46	26	b	b	b	b	b
1084	55	62	65	65	54	34	26	32	33	23	7
1091	62	65	58	54	43	34	b	b	b	b	b
1097	67	59	60	59	46	33	18	33	23	33	24
1102	57	66	70	62	47	46	b	b	b	b	b
1104	58	67	65	64	43	37	30	25	24	14	18
1112	55	61	63	66	44	37	b	b	b	b	b
1113	67	65	66	53	51	39	30	25	22	18	28
1125	59	59	62	50	49	30	b	b	b	b	b
1127	59	59	62	55	51	40	20	43	30	25	17
1135	55	56	62	45	44	26	b	b	b	b	b
1136	65	65	65	67	48	39	24	35	-7	40	23
1146	56	63	68	61	47	57	b	b	b	b	b
1148	62	65	69	52	53	40	29	26	25	20	19
1152	57	58	61	43	41	39	b	b	b	b	b
1153	57	41	79	52	57	37	25	36	28	27	10
1161	54	59	62	52	49	40	b	b	b	b	b
1162	60	62	67	56	48	47	21	37	32	19	20
1173	55	58	48	26	51	38	b	b	b	b	b
1174	61	61	59	48	41	25	20	23	15	21	10
1185	57	70	55	60	49	47	b	b	b	b	b
1189	59	65	65	51	50	46	16	23	19	32	19
1192	65	68	74	67	51	52	b	b	b	b	b
1193	63	62	67	63	53	48	32	37	18	27	24
1202	57	59	59	57	50	49	b	b	b	b	b
1203	52	63	63	57	33	37	17	33	21	19	9

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1214	65	72	61	23	52	51	b	b	b	b	b
1215	65	71	77	67	66	56	44	37	32	39	-70
1223	56	67	67	59	50	41	b	b	b	b	b
1226	53	57	55	48	44	31	27	20	16	7	21
1233	61	71	74	72	65	56	b	b	b	b	b
1236	56	62	59	35	61	45	33	43	25	29	11
1242	50	61	61	56	48	52	b	b	b	b	b
1248	54	66	66	67	59	45	36	30	29	31	23
1251	63	59	70	53	41	52	b	b	b	b	b
12515	61	67	69	56	51	38	40	33	24	13	24
MEAN	58	61	64	56	48	40	28	33	24	23	14
S.D.	4.3	5.9	6.0	10.0	6.6	8.2	7.6	6.5	8.9	8.2	18.5
N	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1011	b	b
1013	20	8
1021	b	b
1024	15	14
1032	b	b
1036	26	13
1043	b	b
1047	25	2
1052	b	b
1054	21	12
1065	b	b
1066	14	9
1071	b	b
1072	17	5
1083	b	b
1084	19	22
1091	b	b
1097	18	7
1102	b	b
1104	21	12
1112	b	b
1113	13	20
1125	b	b
1127	25	12
1135	b	b
1136	30	21
1146	b	b
1148	--	--
1152	b	b
1153	--	--
1161	b	b
1162	--	--
1173	b	b
1174	--	--
1185	b	b
1189	--	--
1192	b	b
1193	--	--
1202	b	b
1203	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
--:Data Unavailable.

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1214	b	b
1215	--	--
1223	b	b
1226	--	--
1233	b	b
1236	--	--
1242	b	b
1248	--	--
1251	b	b
12515	--	--
MEAN	20	12
S.D.	5.1	6.1
N	13	13

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1264	73	70	70	67	55	46	b	b	b	b	b
1267	68	57	60	60	26	24	23	28	15	26	15
1275	33	76	62	55	41	38	b	b	b	b	b
1277	39	77	67	66	49	42	22	35	26	18	24
1283	63	67	70	59	48	46	b	b	b	b	b
1286	57	67	71	71	57	49	39	41	23	17	30
1295	48	59	66	57	48	50	b	b	b	b	b
1296	57	67	79	70	45	26	35	41	31	27	21
1307	61	61	73	65	48	44	b	b	b	b	b
1309	59	57	68	61	47	22	23	33	18	16	24
1311	66	67	74	58	31	48	b	b	b	b	b
1312	59	66	70	61	52	39	26	31	28	28	22
1322	65	65	69	68	50	53	b	b	b	b	b
1323	67	74	68	59	18	77	25	39	22	36	21
1331	54	58	53	58	41	38	b	b	b	b	b
1333	53	65	52	52	42	35	27	30	24	24	9
1341	55	58	58	48	37	27	b	b	b	b	b
1343	66	62	69	59	52	37	31	36	-10	50	15
1353	58	60	67	60	50	42	b	b	b	b	b
1354	47	34	63	58	48	34	31	27	25	16	25
1361	60	64	66	61	54	38	b	b	b	b	b
1365	65	66	72	58	56	34	35	31	40	14	17
1375	50	56	54	47	40	32	b	b	b	b	b
1379	54	61	58	59	49	26	34	29	17	22	11
1382	65	61	62	57	48	35	b	b	b	b	b
1383	62	66	66	48	49	29	35	32	29	18	14
1392	60	58	54	57	39	38	b	b	b	b	b
1394	63	61	63	60	45	38	30	36	24	26	20
1401	54	63	68	65	54	43	b	b	b	b	b
1404	46	51	67	50	47	39	16	28	30	24	26
1414	56	69	69	62	55	40	b	b	b	b	b
1415	58	65	59	58	41	38	10	42	25	27	20
1421	56	56	70	54	51	39	b	b	b	b	b
1428	55	65	81	65	70	60	35	33	36	25	37
1432	62	67	73	64	60	48	b	b	b	b	b
1434	65	66	74	-10	-47	127	80	41	36	32	33
1443	56	63	69	63	44	40	b	b	b	b	b
1444	59	56	56	49	46	34	25	30	19	13	24
1452	59	72	67	66	56	45	b	b	b	b	b
1454	59	66	64	68	53	36	23	41	26	34	23

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1461	62	66	65	66	47	51	b	b	b	b	b
1463	53	74	59	40	46	47	32	32	29	26	21
1474	28	75	64	66	53	39	b	b	b	b	b
1475	61	66	66	63	54	-8	47	51	35	26	36
1483	61	71	64	66	45	36	b	b	b	b	b
1484	59	68	72	64	50	41	33	25	20	-109	100
1491	61	76	82	81	81	67	b	b	b	b	b
1493	60	65	67	52	27	35	18	22	17	16	16
1501	54	64	61	55	47	33	b	b	b	b	b
1503	57	64	53	57	49	35	28	31	24	33	8
MEAN	57	64	66	58	46	41	31	34	24	19	24
S.D.	8.2	7.3	6.9	12.2	16.7	17.3	12.9	6.5	9.7	28.0	17.4
N	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1264	b	b
1267	6	13
1275	b	b
1277	5	23
1283	b	b
1286	18	20
1295	b	b
1296	15	14
1307	b	b
1309	14	13
1311	b	b
1312	24	9
1322	b	b
1323	27	19
1331	b	b
1333	30	17
1341	b	b
1343	28	14
1353	b	b
1354	14	10
1361	b	b
1365	19	20
1375	b	b
1379	19	12
1382	b	b
1383	9	9
1392	b	b
1394	--	--
1401	b	b
1404	--	--
1414	b	b
1415	--	--
1421	b	b
1428	--	--
1432	b	b
1434	--	--
1443	b	b
1444	--	--
1452	b	b
1454	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
–:Data Unavailable.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-M SEX: MALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1461	b	b
1463	--	--
1474	b	b
1475	--	--
1483	b	b
1484	--	--
1491	b	b
1493	--	--
1501	b	b
1503	--	--
MEAN	18	15
S.D.	8.1	4.6
N	13	13

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1511	56	61	69	57	50	36	b	b	b	b	b
1515	57	58	71	59	46	25	22	38	15	28	14
1523	64	65	71	66	56	47	b	b	b	b	b
1524	62	60	70	60	51	38	25	30	22	-109	102
1532	59	61	66	59	37	36	b	b	b	b	b
1533	47	51	69	51	46	37	22	35	24	21	14
1542	48	54	61	58	33	41	b	b	b	b	b
1544	44	57	62	59	54	48	21	36	22	9	32
1554	61	64	80	63	69	54	b	b	b	b	b
1555	62	62	72	66	49	46	28	29	38	19	15
1561	63	65	71	57	49	47	b	b	b	b	b
1566	64	69	77	66	47	37	18	27	24	19	23
1571	61	62	74	58	58	42	b	b	b	b	b
1574	65	54	71	55	48	34	27	25	25	24	7
1584	59	63	75	60	47	40	b	b	b	b	b
1585	55	61	70	60	41	33	14	23	27	22	19
1603	52	64	55	63	43	43	b	b	b	b	b
1605	59	63	58	64	44	44	25	33	26	19	22
1611	53	50	59	51	51	35	b	b	b	b	b
1612	51	54	55	49	40	30	22	27	20	16	19
1622	55	62	69	54	54	38	b	b	b	b	b
1625	63	62	66	58	49	40	28	33	27	22	21
1634	56	62	68	55	49	56	b	b	b	b	b
1636	56	67	57	54	45	40	26	38	18	23	21
1644	53	55	65	57	4	55	b	b	b	b	b
1646	48	51	65	46	47	41	24	32	28	33	28
1652	60	67	67	49	49	44	b	b	b	b	b
1658	62	58	67	52	47	34	35	26	23	25	20
1661	50	59	63	56	44	43	b	b	b	b	b
1664	55	60	66	50	45	31	31	29	27	26	27
1672	59	60	75	58	49	41	b	b	b	b	b
1673	63	63	81	60	54	47	46	31	41	22	28
1681	63	68	83	62	57	48	b	b	b	b	b
1685	58	68	71	66	66	49	30	48	27	26	24
1691	55	56	59	39	38	5	b	b	b	b	b
1692	58	60	72	47	46	41	18	29	19	22	23
1704	56	64	66	49	44	33	b	b	b	b	b
1706	56	65	57	50	37	33	23	25	18	30	17
1714	56	59	65	58	44	41	b	b	b	b	b
1715	65	64	67	64	46	38	26	19	27	16	13

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

Note: There was no litter F1 litter No. 159 since F0 dam No. 159 was not pregnant.

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1723	50	56	57	44	44	46	b	b	b	b	b
1727	46	62	61	66	57	43	24	46	23	8	25
1733	58	66	68	63	53	54	b	b	b	b	b
1734	70	75	70	63	61	50	30	29	26	16	26
1741	68	71	73	56	52	54	b	b	b	b	b
1743	67	67	68	57	49	45	25	40	35	20	31
1754	55	60	62	57	44	39	b	b	b	b	b
1755	59	60	65	47	49	47	37	40	23	29	27
MEAN	58	61	67	57	48	41	26	32	25	16	25
S.D.	5.9	5.2	6.6	6.4	9.5	8.8	6.7	7.1	6.1	27.3	17.5
N	48	48	48	48	48	48	24	24	24	24	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1511	b	b
1515	29	7
1523	b	b
1524	32	20
1532	b	b
1533	19	11
1542	b	b
1544	21	13
1554	b	b
1555	27	17
1561	b	b
1566	14	14
1571	b	b
1574	21	12
1584	b	b
1585	8	11
1603	b	b
1605	25	16
1611	b	b
1612	18	14
1622	b	b
1625	21	21
1634	b	b
1636	--	--
1644	b	b
1646	--	--
1652	b	b
1658	--	--
1661	b	b
1664	--	--
1672	b	b
1673	--	--
1681	b	b
1685	--	--
1691	b	b
1692	--	b
1704	b	b
1706	--	--
1714	b	b
1715	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
–:Data Unavailable.

Note: There was no litter F1 litter No. 159 since F0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-M SEX: MALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1723	b	b
1727	--	--
1733	b	b
1734	--	--
1741	b	b
1743	--	--
1754	b	b
1755	--	--
MEAN	21	14
S.D.	6.8	4.1
N	11	11

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1762	59	59	62	53	44	39	b	b	b	b	b
1763	61	60	60	60	47	41	31	26	23	28	16
1773	61	65	63	55	44	41	b	b	b	b	b
1774	57	60	68	56	43	33	16	31	22	24	24
1782	57	66	56	60	38	32	b	b	b	b	b
1783	55	63	64	58	49	42	25	30	19	15	14
1792	55	56	70	63	56	29	b	b	b	b	b
1795	56	53	56	55	40	31	22	26	19	24	17
1801	55	55	57	66	53	47	b	b	b	b	b
1806	57	57	66	-18	85	52	40	34	31	29	22
1813	54	56	60	62	40	36	b	b	b	b	b
1814	55	58	64	58	45	45	27	29	24	16	17
1823	55	58	38	13	69	50	b	b	b	b	b
1824	53	55	69	59	47	51	27	32	29	22	28
1831	60	67	69	60	39	36	b	b	b	b	b
1835	55	65	66	57	46	41	32	37	30	24	19
1845	54	60	64	60	48	34	b	b	b	b	b
1846	47	61	58	60	51	47	34	41	27	24	20
1852	56	61	60	61	55	38	b	b	b	b	b
1853	63	69	72	71	54	49	32	45	29	24	22
1861	59	56	61	52	48	17	b	b	b	b	b
1865	49	45	46	44	33	21	21	28	22	15	9
1873	52	51	64	58	47	28	b	b	b	b	b
1875	53	61	59	44	41	32	28	25	29	19	21
1882	60	65	72	65	58	58	b	b	b	b	b
1883	60	60	59	61	43	41	24	30	26	13	21
1894	60	68	78	58	60	44	b	b	b	b	b
1897	52	55	62	50	42	28	5	40	29	25	23
1901	58	62	55	59	46	39	b	b	b	b	b
1904	57	58	57	55	46	36	27	28	24	24	18
1912	54	54	71	60	56	16	b	b	b	b	b
1914	54	67	77	58	61	50	12	34	36	44	24
1921	56	52	68	55	60	41	b	b	b	b	b
1924	51	56	65	67	55	52	25	40	36	23	25
1934	53	60	64	57	58	48	b	b	b	b	b
1936	53	56	63	52	55	43	22	38	32	22	23
1941	54	57	66	62	43	41	b	b	b	b	b
1942	72	68	72	68	52	38	36	38	33	32	26
1952	51	60	61	60	57	41	b	b	b	b	b
1956	56	65	60	61	47	36	27	31	26	21	19

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
1962	55	55	54	49	35	31	b	b	b	b	b
1965	56	60	58	55	52	29	24	26	19	18	13
1972	53	63	60	60	47	34	b	b	b	b	b
1974	48	59	50	52	50	43	21	30	36	24	18
1982	56	58	62	57	45	40	b	b	b	b	b
1988	58	64	64	55	47	34	28	22	27	23	9
1991	49	60	68	62	65	52	b	b	b	b	b
1993	50	61	64	60	58	41	25	40	26	26	21
2005	58	61	55	60	42	35	b	b	b	b	b
2008	60	60	61	53	45	37	15	23	26	19	18
MEAN	56	60	62	56	50	39	25	32	27	23	19
S.D.	4.3	4.8	7.2	13.5	9.2	8.9	7.6	6.3	5.1	6.3	4.8
N	50	50	50	50	50	50	25	25	25	25	25

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1762	b	b
1763	21	15
1773	b	b
1774	17	15
1782	b	b
1783	14	9
1792	b	b
1795	20	7
1801	b	b
1806	27	12
1813	b	b
1814	18	10
1823	b	b
1824	21	17
1831	b	b
1835	25	8
1845	b	b
1846	19	24
1852	b	b
1853	30	27
1861	b	b
1865	24	-28
1873	b	b
1875	19	17
1882	b	b
1883	--	--
1894	b	b
1897	--	--
1901	b	b
1904	--	--
1912	b	b
1914	--	--
1921	b	b
1924	--	--
1934	b	b
1936	--	--
1941	b	b
1942	--	--
1952	b	b
1956	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
--:Data Unavailable.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-M SEX: MALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
1962	b	b
1965	--	--
1972	b	b
1974	--	--
1982	b	b
1988	--	--
1991	b	b
1993	--	--
2005	b	b
2008	--	--
MEAN	21	11
S.D.	4.5	13.8
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
10112	25	45	28	24	11	18	b	b	b	b	b
10113	29	50	33	28	23	16	41	45	60	-83	38
10214	44	43	17	20	29	7	b	b	b	b	b
10217	42	42	25	31	12	30	17	46	73	-63	-10
10315	39	23	28	24	14	15	b	b	b	b	b
10318	41	29	12	37	29	19	26	39	59	-68	12
10412	37	37	32	-17	39	21	b	b	b	b	b
10413	38	28	14	36	14	18	38	41	76	-102	-10
10511	34	28	19	24	9	10	b	b	b	b	b
10513	45	28	22	23	16	13	39	34	-20	b	b
10614	39	38	20	18	20	15	b	b	b	b	b
10616	35	28	20	17	14	18	26	40	76	-87	17
10712	40	34	29	25	15	15	b	b	b	b	b
10713	39	37	26	22	34	33	39	42	68	-64	31
10813	43	25	23	22	16	11	b	b	b	b	b
10815	41	26	16	28	19	10	32	32	67	-73	0
10911	42	38	23	19	9	26	30	38	76	-84	11
11012	43	44	21	34	23	27	b	b	b	b	b
11015	44	43	30	31	23	28	41	49	91	-105	-8
11111	39	41	27	17	11	21	b	b	b	b	b
11117	42	31	27	19	22	14	31	35	80	-92	10
11212	43	27	22	14	14	19	b	b	b	b	b
11213	42	35	27	21	22	19	28	37	95	-104	3
11315	33	43	1	43	31	11	b	b	b	b	b
11316	49	37	37	23	18	17	31	37	84	-88	25
11412	43	33	31	14	26	17	b	b	b	b	b
11414	47	27	37	25	28	22	35	43	69	-85	33
11511	39	33	26	17	12	2	b	b	b	b	b
11519	46	32	22	19	22	18	35	34	84	-94	12
11611	46	29	31	10	19	15	b	b	b	b	b
11612	43	30	29	24	32	13	38	32	75	-91	-3
11711	34	35	13	22	10	21	b	b	b	b	b
11712	36	30	19	15	15	11	40	35	70	-113	18
11812	48	36	23	8	7	34	b	b	b	b	b
11814	40	26	18	21	16	11	32	40	72	-67	-3
11911	51	45	32	21	20	18	b	b	b	b	b
11915	49	38	23	29	14	17	26	11	15	b	b
12012	47	29	23	26	20	14	b	b	b	b	b
12013	42	41	29	6	35	21	29	34	48	-50	40
12113	42	35	27	22	24	28	b	b	b	b	b

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70. There was only one female in litter No. 109.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
12114	46	38	33	20	19	18	48	30	69	-71	-6
12211	33	29	22	16	19	16	b	b	b	b	b
12213	41	33	29	19	17	19	27	32	93	-115	-6
12312	40	24	31	18	12	18	b	b	b	b	b
12313	38	30	22	16	17	14	33	37	83	-103	4
12411	42	34	34	7	8	24	b	b	b	b	b
12413	40	38	31	26	22	22	32	23	-4	b	b
12511	49	22	37	23	19	24	b	b	b	b	b
12519	50	36	22	30	23	13	39	32	47	-39	-12
MEAN	41	34	25	21	19	18	33	36	64	-84	9
S.D.	5.3	6.6	7.1	9.3	7.4	6.4	6.7	7.7	28.4	20.0	16.4
N	49	49	49	49	49	49	25	25	25	22	22

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
10112	b	b
10113	6	-6
10214	b	b
10217	5	-12
10315	b	b
10318	16	26
10412	b	b
10413	12	5
10511	b	b
10513	b	b
10614	b	b
10616	10	-7
10712	b	b
10713	0	-1
10813	b	b
10815	-1	15
10911	7	-4
11012	b	b
11015	16	7
11111	b	b
11117	11	-1
11212	b	b
11213	4	5
11315	b	b
11316	-1	14
11412	b	b
11414	--	--
11511	b	b
11519	--	--
11611	b	b
11612	--	--
11711	b	b
11712	--	--
11812	b	b
11814	--	--
11911	b	b
11915	b	b
12012	b	b
12013	--	--
12113	b	b

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
--:Data Unavailable.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
12114	--	--
12211	b	b
12213	--	--
12312	b	b
12313	--	--
12411	b	b
12413	b	b
12511	b	b
12519	--	--
MEAN	7	3
S.D.	6.1	10.9
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
12611	44	28	34	27	21	11	b	b	b	b	b
12612	47	38	26	38	18	21	36	36	88	-123	19
12715	42	33	23	22	26	10	b	b	b	b	b
12716	42	33	29	28	26	12	43	43	94	-124	14
12813	42	43	25	33	20	25	b	b	b	b	b
12815	41	37	30	44	18	26	26	35	49	-53	36
12911	40	33	31	25	24	19	b	b	b	b	b
12912	38	29	34	26	16	22	24	21	-8	4	b
13D11	44	34	25	24	12	18	b	b	b	b	b
13013	55	44	33	37	30	-92	106	58	66	-66	11
13113	44	37	22	19	23	18	b	b	b	b	b
13114	48	38	23	27	15	19	35	36	78	-104	28
13212	49	28	40	23	16	25	b	b	b	b	b
13213	46	28	3D	25	14	14	41	45	51	-6D	3
13315	43	33	24	23	26	15	b	b	b	b	b
13317	40	35	27	32	23	22	38	39	83	-116	21
13412	39	29	3D	20	22	19	b	b	b	b	b
13414	46	34	27	30	25	20	32	26	77	-82	7
13512	37	26	22	30	18	20	b	b	b	b	b
13515	4D	31	26	27	7	18	26	29	110	-126	18
13612	45	37	2D	34	21	22	b	b	b	b	b
13614	45	41	34	25	16	15	42	37	88	-103	10
13711	32	32	19	28	22	11	b	b	b	b	b
13713	44	30	34	26	16	15	39	30	49	-42	2
13811	42	42	20	35	22	33	b	b	b	b	b
13815	50	33	20	33	23	19	38	44	79	-94	7
13912	47	33	4	48	16	16	b	b	b	b	b
13913	36	4D	23	20	12	24	48	32	88	-1D5	-6
14D11	42	28	31	17	22	11	b	b	b	b	b
14014	41	30	35	12	24	14	30	38	93	-97	3
14111	42	42	26	23	32	25	b	b	b	b	b
14112	41	35	39	23	23	11	28	37	45	-43	-3
14212	42	29	36	12	16	15	b	b	b	b	b
14213	48	32	28	28	21	21	27	29	48	-42	10
14314	49	37	34	21	28	25	b	b	b	b	b
14315	40	33	30	22	14	25	39	41	55	-67	46
14412	39	36	28	17	21	14	31	28	70	-89	6
14416	44	32	24	28	22	-54	b	b	b	b	b
14511	46	39	30	20	24	14	b	b	b	b	b
14514	51	40	20	30	23	25	28	32	61	-64	4

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
14613	46	36	35	23	19	1	b	b	b	b	b
14615	44	25	36	37	15	11	38	45	64	-80	2
14712	47	29	27	24	18	14	b	b	b	b	b
14714	48	40	29	32	26	27	24	43	61	-68	3
14811	47	37	13	30	14	12	b	b	b	b	b
14812	43	45	25	18	28	23	32	43	63	-61	8
14913	49	33	26	27	19	24	b	b	b	b	b
14916	48	27	32	31	21	29	52	54	96	-129	33
15011	40	35	31	17	18	13	b	b	b	b	b
15013	42	29	26	17	9	26	26	30	65	-71	8
MEAN	44	34	28	26	20	15	37	37	69	-80	12
S.D.	4.2	5.0	6.6	7.4	5.3	19.5	16.2	8.6	23.8	32.6	12.8
N	50	50	50	50	50	50	25	25	25	25	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
12611	b	b
12612	13	17
12715	b	b
12716	22	9
12813	b	b
12815	1	13
12911	b	b
12912	b	b
13011	b	b
13013	17	-6
13113	b	b
13114	2	1
13212	b	b
13213	7	14
13315	b	b
13317	20	10
13412	b	b
13414	20	13
13512	b	b
13515	4	-2
13612	b	b
13614	3	14
13711	b	b
13713	7	10
13811	b	b
13815	8	15
13912	b	b
13913	--	--
14011	b	b
14014	--	--
14111	b	b
14112	--	--
14212	b	b
14213	--	--
14314	b	b
14315	--	--
14412	--	--
14416	b	b
14511	b	b
14514	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
--:Data Unavailable.

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 2-F SEX: FEMALE
DOSE: 2 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
14613	b	b
14615	--	--
14712	b	b
14714	--	--
14811	b	b
14812	--	--
14913	b	b
14916	--	--
15011	b	b
15013	--	--
MEAN	10	9
S.D.	7.7	7.3
N	12	12

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
15112	34	35	25	21	28	18	b	b	b	b	b
15115	46	37	28	34	22	20	33	38	61	-65	-4
15211	37	36	17	25	12	12	b	b	b	b	b
15213	46	32	28	23	16	19	29	29	62	-48	20
15313	42	35	17	27	9	29	b	b	b	b	b
15314	39	36	23	29	19	14	35	33	57	-53	21
15412	40	38	30	22	23	25	b	b	b	b	b
15416	42	31	27	25	25	19	20	35	83	-72	19
15513	43	41	31	34	25	25	b	b	b	b	b
15518	49	37	23	-56	81	17	27	40	59	-51	28
15611	48	41	38	31	21	29	b	b	b	b	b
15617	47	36	27	43	19	32	30	35	82	-85	36
15712	38	29	34	20	18	9	b	b	b	b	b
15714	46	32	28	15	27	19	46	43	91	-102	2
15814	39	38	29	29	21	33	b	b	b	b	b
15816	47	37	21	36	24	25	6	33	51	103	-128
16011	39	34	24	22	19	21	b	b	b	b	b
16015	37	33	22	21	14	15	34	26	64	-61	4
16113	38	33	23	16	27	19	b	b	b	b	b
16114	43	37	20	14	22	13	39	32	75	-84	-1
16211	23	48	22	16	17	22	b	b	b	b	b
16216	25	40	15	19	17	19	31	38	67	-80	26
16311	42	33	26	16	21	15	b	b	b	b	b
16313	36	39	17	23	16	12	34	52	68	-94	15
16412	39	31	24	19	15	17	b	b	b	b	b
16413	48	33	34	20	21	24	32	35	45	-47	11
16513	44	36	41	26	25	15	b	b	b	b	b
16514	47	47	37	26	23	21	29	40	95	-106	21
16613	44	27	25	14	11	7	b	b	b	b	b
16614	44	33	31	17	20	13	32	30	67	-90	7
16711	46	31	20	24	24	13	b	b	b	b	b
16714	44	34	19	19	18	9	44	31	40	54	-51
16813	42	46	26	31	25	21	b	b	b	b	b
16814	43	38	22	-43	81	12	46	39	60	-65	5
16911	42	25	28	10	17	10	b	b	b	b	b
16913	42	34	31	23	1	20	27	35	99	-122	16
17016	45	28	29	17	22	19	b	b	b	b	b
17018	44	32	24	26	18	18	25	27	85	-100	18
17111	44	32	26	18	20	15	b	b	b	b	b
17115	42	31	20	31	19	17	29	32	68	-59	1

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

Note: There was no litter F1 litter No. 159 since F0 dam No. 159 was not pregnant.

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
17212	46	37	21	23	25	16	b	b	b	b	b
17215	41	33	29	27	16	14	21	22	50	-56	5
17311	54	54	31	26	26	22	b	b	b	b	b
17312	43	26	20	21	3	15	37	39	89	-98	8
17411	48	44	35	32	28	20	b	b	b	b	b
17413	46	39	28	-24	80	21	52	34	47	-62	23
17513	43	37	31	20	22	32	b	b	b	b	b
17516	40	31	27	20	24	17	35	31	93	-120	24
MEAN	42	36	26	19	23	19	32	35	69	-65	5
S.D.	5.4	5.7	5.8	17.3	16.0	6.1	9.6	6.2	17.1	50.1	32.9
N	48	48	48	48	48	48	24	24	24	24	24

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
15112	b	b
15115	-8	12
15211	b	b
15213	-5	-4
15313	b	b
15314	0	-6
15412	b	b
15416	-9	-6
15513	b	b
15518	10	8
15611	b	b
15617	0	11
15712	b	b
15714	12	0
15814	b	b
15816	-8	25
16011	b	b
16015	1	10
16113	b	b
16114	3	-6
16211	b	b
16216	-8	-7
16311	b	b
16313	--	--
16412	b	b
16413	--	--
16513	b	b
16514	--	--
16613	b	b
16614	--	--
16711	b	b
16714	--	--
16813	b	b
16814	--	--
16911	b	b
16913	--	--
17016	b	b
17018	--	--
17111	b	b
17115	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
–:Data Unavailable.

Note: There was no litter F1 litter No. 159 since F0 dam No. 159 was not pregnant.

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 3-F SEX: FEMALE
DOSE: 6 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
17212	b	b
17215	--	--
17311	b	b
17312	--	--
17411	b	b
17413	--	--
17513	b	b
17516	--	--
MEAN	-1	3
S.D.	7.3	10.5
N	11	11

--: Data Unavailable b: Scheduled Sacrifice

ORAL PRENATAL AND POSTNATAL DEVELOPMENT
STUDY OF WR238605 SUCCINATE IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
17614	39	30	29	27	19	7	b	b	b	b	b
17616	36	35	22	24	21	12	35	14	-10	b	b
17712	46	30	26	22	21	17	b	b	b	b	b
17713	41	34	23	22	22	15	35	39	62	-89	21
17815	42	25	18	29	11	10	b	b	b	b	b
17816	42	30	25	25	19	16	39	44	33	-34	-4
17911	36	30	18	40	21	8	b	b	b	b	b
17912	41	34	21	28	19	19	37	41	67	-75	-3
18013	37	40	22	24	24	23	b	b	b	b	b
18014	37	30	27	25	20	20	53	34	85	-100	7
18112	30	23	23	18	12	9	b	b	b	b	b
18116	27	32	16	15	5	12	39	49	83	-119	-2
18213	33	24	25	20	18	17	b	b	b	b	b
18214	37	28	28	18	27	19	42	41	82	-78	9
18315	41	44	29	32	32	23	b	b	b	b	b
18317	34	37	26	32	19	16	37	38	99	-92	19
18411	37	26	24	20	14	15	b	b	b	b	b
18416	42	34	29	21	19	23	42	52	90	-121	19
18511	43	30	28	33	22	20	b	b	b	b	b
18515	40	32	15	39	26	21	25	50	71	-66	14
18611	42	27	19	21	15	8	b	b	b	b	b
18613	31	27	22	16	15	16	5	49	81	-79	7
18712	41	27	22	23	22	11	b	b	b	b	b
18714	40	26	29	17	27	18	32	41	75	-95	6
18812	48	38	24	25	27	14	b	b	b	b	b
18815	51	37	31	46	30	24	27	13	21	b	b
18911	43	44	38	33	30	11	b	b	b	b	b
18912	42	39	38	30	31	19	20	30	31	9	7
19012	44	40	20	23	19	19	b	b	b	b	b
19019	45	37	22	25	20	12	41	25	74	-91	15
19112	52	33	33	23	26	16	b	b	b	b	b
19114	47	33	33	18	30	22	36	36	82	-87	21
19214	38	32	33	22	20	8	b	b	b	b	b
19215	39	32	28	22	26	13	31	33	57	-40	0
19315	48	42	32	28	24	31	b	b	b	b	b
19317	42	34	32	13	34	23	35	47	85	-106	16
19415	43	29	26	23	16	21	b	b	b	b	b
19416	51	23	30	20	20	16	31	39	68	-72	5
19512	37	40	34	23	18	28	b	b	b	b	b
19514	39	36	24	25	21	13	28	46	75	-73	5

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 35[c]	PND 42	PND 49	PND 56	PND 63	PND 70	PND 77[d]	PND 84	PND 91	PND 98	PND 105
19613	45	24	24	12	22	25	b	b	b	b	b
19617	40	32	27	29	23	20	30	48	60	-68	13
19715	40	31	23	16	14	7	b	b	b	b	b
19716	43	40	19	25	19	14	35	41	72	-90	7
19812	42	35	31	29	26	27	♀	28	17	b	b
19814	47	41	30	22	12	-43	b	b	b	b	b
19912	37	37	25	30	18	24	b	b	b	b	b
19915	36	35	18	25	19	16	31	35	82	-105	20
20011	41	39	31	31	13	-12	b	b	b	b	b
20012	48	51	19	30	11	26	29	33	85	-88	4
MEAN	41	33	26	25	21	15	32	38	65	-80	9
S.D.	5.3	6.1	5.5	6.7	6.1	11.0	10.1	10.2	26.6	29.1	8.0
N	50	50	50	50	50	50	25	25	25	22	22

--: Data Unavailable b: Scheduled Sacrifice

[a]Weight gains compared to the previous period.
[c]Baseline is PND28. Two animals/sex/litter were evaluated from PND28 - 70.
[d]One animal/sex/litter was evaluated from PND70 - scheduled sacrifice (i.e., during the fertility phase).

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a] (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
17614	b	b
17616	b	b
17712	b	b
17713	12	-2
17815	b	b
17816	1	7
17911	b	b
17912	8	9
18013	b	b
18014	-3	14
18112	b	b
18116	3	-6
18213	b	b
18214	13	0
18315	b	b
18317	-9	-2
18411	b	b
18416	-1	6
18511	b	b
18515	9	15
18611	b	b
18613	-1	-5
18712	b	b
18714	12	4
18812	b	b
18815	b	b
18911	b	b
18912	b	b
19012	b	b
19019	--	--
19112	b	b
19114	--	--
19214	b	b
19215	--	--
19315	b	b
19317	--	--
19415	b	b
19416	--	--
19512	b	b
19514	--	--

[a]Weight gains compared to the previous period.
[b]Scheduled Sacrifice.
--:Data Unavailable.

INDIVIDUAL WEIGHT GAIN (Grams) (Postweaning Period)

STUDY: 200L GROUP: 4-F SEX: FEMALE
DOSE: 18 (mg base/kg/day)

ANIMAL #	PND 112	PND 119
19613	b	b
19617	--	--
19715	b	b
19716	--	--
19812	b	b
19814	b	b
19912	b	b
19915	--	--
20011	b	b
20012	--	--
MEAN	4	4
S.D.	7.3	7.3
N	11	11

--: Data Unavailable b: Scheduled Sacrifice